EXHIBIT B

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC. PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LIGITATION	**Master File No. 2:12-MD-02327** **MDL No. 2327**
THIS DOCUMENT RELATES TO PLAINTIFFS: **Wave 1 Cases**	**JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

RULE 26 EXPERT REPORT OF PROF. DR. MED. UWE KLINGE

I. SUMMARY OF OPINIONS

Based on my background training and experience as a general and abdominal surgeon who used Prolene mesh for hernia repair in patients and treated Prolene-mesh-related complications in patients, and based on over 20 years of studying Prolene and other surgical meshes as a biomaterials scientist, 10 years of which were as a consultant to Ethicon regarding safe mesh design in their preclinical studies of Prolene and other surgical meshes, performing histopathological analysis on hundreds of explanted hernia, sling and prolapse meshes, being an invited lecturer at conferences around the world on the topic of surgical meshes, authoring or co-authoring over 100 peer-reviewed publications regarding surgical meshes, including numerous ones regarding Prolene mesh, reviewing thousands of pages of scientific literature, thousands of pages of internal Ethicon documents and thousands of pages of deposition testimony, the following is a summary of my opinions in this case, all of which I hold to a reasonable degree of medical and scientific certainty.[1]

The Prolene mesh in TVT undergoes a Chronic FBR.

After implantation of the TVT mesh, there is a chronic (permanent) foreign body reaction in a woman's pelvic tissue whereby the woman's body will react to the polypropylene indefinitely, creating a chronic inflammatory response that leads to scarring around the mesh fibers. Claims by Ethicon in its TVT Instructions for Use (IFU) that "a transient foreign body response may occur" and in its TVT marketing brochures that there is "[n]o foreign body reaction after PROLENE mesh implantation" are inconsistent, false and misleading, and Ethicon knew or should have been known them to be untrue at the time the company employees wrote these documents and certainly prior to the launch of TVT in 1998.

[1] Because the material used in Ethicon's incontinence repair meshes is of identical construction, i.e., so-called "Old Construction" 6 mil Prolene, with certain exceptions as noted herein, the acronym "TVT" will be used throughout this report to represent the entire TVT incontinence sling product line by Ethicon.

The weight (surface area) of the Prolene mesh in TVT unnecessarily increases the risk of patient injury versus lighter weight mesh design.

The greater the surface area of a medical implant, the greater the foreign body reaction and the inflammatory response. Ethicon had critical mesh design information regarding the negative consequences in the human tissue of heavy weight, small pore meshes beginning as early as 1998. The heavy weight Prolene mesh (105-110 g/m2) in Ethicon's TVT products is many times stronger than it needs to be for its intended purpose of treating stress urinary incontinence and thus, it is "overengineered" and leaves much more polymer material in a woman's delicate and sensitive pelvic tissues than is necessary. It is my opinion to a reasonable degree of medical and scientific certainty that any pelvic mesh designed with this much excess surface area and weight unreasonably and unnecessarily increases the risk of injury to the patient and is a less safe design than lighter weight mesh as it causes an unnecessarily increased FBR and inflammatory response

The distance between the fibers of the Prolene mesh in TVT unnecessarily increases the risk of patient injury versus mesh design with a larger distance between the fibers.

The smaller the distance between the fibers of a mesh implant, the greater the risk of scar tissue forming in the pores ("bridging fibrosis" or "fibrotic bridging"). As early as 1998, and certainly by the early 2000's, Ethicon had critical design information that the risk of bridging fibrosis is increased by polypropylene surgical mesh with a distance between the fibers of less than 1mm in all directions, which in turn increases the risk of a rigid scar plate forming throughout the mesh, leading to integration of the entire mesh in scar tissue. Any pelvic mesh designed with pores this small unreasonably and unnecessarily increases the risk of injury to the patient and is a less safe design than mesh with a greater distance between the fibers. The pore size of the Prolene mesh in Ethicon's TVT products is, according to Ethicon, less than 1mm.

It is my opinion to a reasonable degree of medical and scientific certainty that Ethicon's failure to implement new, critical mesh design changes (lighter weight, greater distance between the fibers) in TVT before the launch of TVT-R in 1998 was unreasonable; it unnecessarily compromised patient safety; and it has led to patient complications like chronic inflammatory reaction, excessive scarring through and around the mesh, nerve entrapment, chronic pain, dyspareunia, erosions, recurrence and the necessity of reoperation in an attempt to correct these problems. The Prolene mesh in Ethicon's TVT products is unsuitable for use as a permanent implant for treatment of a woman's stress urinary incontinence. Ethicon did not act as a reasonable manufacturer in choosing to use the "Old Construction 6 mil" Prolene mesh in its TVT products.

The Prolene mesh in TVT undergoes pore deformation under minimal stress.

A knitted surgical mesh device like the TVT that is permanently implanted in human tissue must be designed in such a manner that the pores of the mesh do not collapse and deform upon the expected forces of implantation as well as the expected in vivo forces. Under minimal strain, the TVT mesh pores deform and collapse thereby increasing the risk of injury to patients in which it is implanted and is a less safe design than products that better withstand these conditions and do not display these poor outcomes. It is my opinion to a reasonable degree of medical and scientific certainty that permanent deformation and pore collapse of the TVT mesh leads to

fibrotic bridging, scar plate formation, excessive scarring through and around the mesh and a host of tissue complications that can lead to chronic pain, recurrence, erosions, dyspareunia and need for reoperation, to name a few, making it unnecessarily unsafe for its intended purpose of being permanently implanted in a woman's pelvic tissue.

The Prolene mesh in TVT contracts/shrinks.

The Prolene mesh in Ethicon's TVT products contracts or shrinks 30-50% after implantation. This shrinkage was known in the medical device community prior to the launch of TVT in 1998. It is my opinion to a reasonable degree of medical and scientific certainty that TVT mesh shrinkage, caused by fibrosis leads to nerve entrapment, chronic pelvic pain, erosions, organ dysfunction, recurrence and the need for reoperation to remove some or all of the contracted mesh and excessive scar tissue, thereby making TVT unsuitable for its intended use as a permanent pelvic implant to treat stress urinary incontinence in women.

The Mechanical Cut Prolene Mesh in the TVT products deforms, frays, loses particles, curls and ropes increasing the risk of complications to the patients.

The TVT mesh is a knitted textile design without a border and therefore, as tension is placed on the mesh, its frayed, unbordered edges shed particles of polypropylene before, during and after the surgery. As tension is placed on the mesh, it also curls and ropes causing increased scarring between the fibers. It is my opinion to a reasonable degree of medical and scientific certainty that The release of particles into the surrounding tissue with its increase of surface area and the curled roped mesh all lead to an increased inflammatory response, chronic foreign body reaction, erosions, chronic pelvic pain, failure of the implant, chronic sexual dysfunction and dyspareunia, organ damage, urinary dysfunction, inability to remove the device and the need for surgical intervention.

There are safer alternative pelvic mesh design characteristics than those of TVT.

There are alternative design characteristics of pelvic floor meshes that would be safer in a woman's pelvic tissues as a treatment for incontinence than some of the design characteristics of the Prolene mesh in TVT. The Old Construction TVT MCM Prolene mesh was created in the 1970's, years before Ethicon developed meshes for both hernia repair and pelvic floor repair using safer mesh design. For example, by the late 1990's and early 2000's, the technology of surgical meshes had evolved to produce meshes that were lighter weight, had greater distance between the fibers, had better stability under stress, had laser cut edges and had a different polymer material. Ethicon began marketing lighter weight meshes with larger distance between the fibers as early as 1998 and continued to advance this technology in its hernia and certain pelvic floor repair mesh products through 2002. It had designed meshes with a different polymer (PVDF) by at least 2002 and meshes that were laser cut by 1998, including TVT laser cut samples.[2] Ethicon knew in 1999 that the TVT with the laser cut mesh had a marked reduction in the amount of loose ends falling off compared to mechanically cut mesh, and is less difficult to deform, facilitating correct placement of the mesh.[3] However, Ethicon has continued to market its 1970's technology Old Construction Prolene mesh in its original TVT-R up to the present date.

---

[2] ETH.MESH.12009078-12009081
[3] ETH.MESH.10182456-10182461

Based upon the opinions above, I am able to conclude, to a reasonable degree of medical and scientific certainty, that the Prolene mesh used in Ethicon's TVT products is designed in such a way that it does in fact unnecessarily cause a greater inflammatory response and greater foreign body reaction in women's pelvic tissues leading to harmful complications in some patients. I am also able to conclude that these materials were inadequately tested and studied before being sold to treat incontinence and that as a result of all of these factors, set forth more fully in this report, the TVT device is not adequately designed to be safely implanted in a woman's pelvis for the rest of her life.

II. BACKGROUND AND QUALIFICATIONS

With regard to my medical training, I attended medical school in Aachen, Germany from 1977 to 1983. I began my medical profession at the surgical department of the University Hospital of the RWTH, Aachen, Germany (Department heads/Mentors: Prof. Reifferscheid - 1985, Schumpelick 1985-2010, Neumann 2010-). From 1995 to 2006, my practice was focused primarily on abdominal surgery, and specifically, hernia repair. As a hernia surgeon, I used textile implants (flat meshes) for the repair of abdominal wall hernia or defects in more than 300 patients; mainly groin hernia, umbilical hernia, incisional hernia and parastomal hernia. Although I never performed surgery for repair of SUI or POP, I implanted and studied the Prolene mesh used in TVT extensively over many years.

In 1993, in addition to my surgical practice, I began focusing on surgical research in the area of biomaterial science including tissue engineering and material characteristics, and I designed preclinical models for safe surgical mesh design, including histopathological analysis. I am the author/co-author of approximately 200 peer-reviewed publications listed in PubMed, over 100 of which involve hernia and/or surgical mesh. I have authored and/or contributed to more than 50 book chapters and have been an invited lecturer to more than 160 speaking engagements/conferences. I have received numerous research grants from various institutions and corporations including several grants from the German Ministry for Education and Research, the Ministry for Economics, the German research foundation DFG, the NRW Ministry for Education and Research, the Interdisciplinary Center for Clinical Research of the University of Aachen (RWTH), as well as from industry (Ethicon, Covidien). (Attached hereto as Appendix "A" is a current copy of my Curriculum Vitae with a list of my publications).

III. BRIEF HISTORY OF TEXTILE MESHES FOR TISSUE REPAIR 1958-1993 – THE ABDOMINAL WALL

The current use of textile meshes is based on Usher who, in 1958, started to publish the successful reinforcement of the abdominal wall in six dogs. Initially, meshes were regarded as an alternative procedure, particularly in big hernias. In 1986, Lichtenstein presented his procedure of mesh implantation as the new standard for groin hernia repair. With this technique, the mesh reinforces the tissue in a so-called "tension free" manner. In the early years, Usher used a knitted structure of polypropylene, later widely known as Marlex®. However, Marlex® had increased stiffness after implantation along with considerable complications. Alternatives to Marlex were the polyester mesh Mersilene® from Ethicon or the ePTFE mesh from Gore.

In the late 1980's and early 1990's, when polypropylene surgical mesh was increasingly used in hernia surgeries, there was a general lack of knowledge about the materials and about the

clinical outcomes associated with these materials. Side effects often manifested with a considerable delay of up to several years. Correspondingly, reports dealing with pain as a major postoperative complication (less than 10% of all hernia publications in PubMed) were published with a delay of years [Fig.1]. We began to look at the scar formation pathologically and developed the theory that incisional hernias could be due to a defective wound healing process with an impaired collagen formation, favoring the necessity to support tissues in these patients by prosthetics.

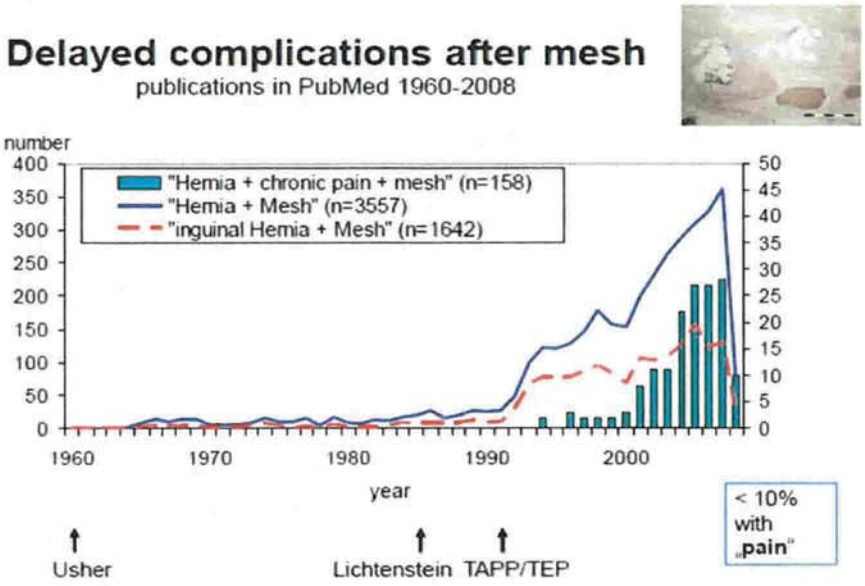


Figure 1

IV. DEVELOPMENT OF THE FIRST LARGE PORE MESH CONSTRUCTION THAT WAS ADAPTED TO PHYSIOLOGICAL REQUIREMENTS

In the early 1990's, we speculated that an adaptation of the strength of surgical meshes to the physiological requirements of the tissues in which they would be implanted may allow a considerable material reduction which could improve biocompatibility. We felt that the textile characterization of meshes at that time did not sufficiently reflect the physicochemical properties of the textile, so we began our work by first identifying the relevant parameters.

In conjunction with various grants, RWTH University initiated a research program to study safe mesh design. Through cooperative efforts with Ethicon and the support by these research grants, the project went on for about 10 years. In this period, we gained significant knowledge about the textiles; we defined standard biomechanical characterization for better comparison of different mesh designs; we established models for testing the tissue response in animals; we looked for parameters that reflected the inflammatory and fibrotic activity of the foreign body reaction; and we developed a technique to quantify the biomechanical impact on, and the biomechanical properties of, tissues.

As our research progressed, we calculated that hernia meshes needed a tensile strength of 16 N/cm and an elasticity of about 20-30% at this strain. Ethicon provided our research team with thin (about 40 µm) polypropylene threads. Because we were provided only with these 40-µm

fibers, we had to combine 5 strands of them at interval distances of 2-3 mm to withstand a strain of 16 N/cm. As this polypropylene net was very floppy, we added an absorbable fiber of Vicryl® (Ethicon) to temporarily make it stiffer. After absorption of the Vicryl®, there remained an open structure with about 30% of the material of the Prolene. This new structure with pores larger than 2 mm, later marketed as Vypro® by Ethicon (1998) and patented in 2000 in the US (6,192,962), was then studied extensively in several experimental studies. The results were presented at several conferences and most of it has been published in PubMed-listed journals. Vypro® was the first truly lightweight, large pore surgical mesh and became the first of the second-generation surgical meshes. This development would become what is known as the "Lightweight Large Pore Concept" which has been adopted by surgical mesh manufacturers worldwide in developing newer generation meshes and was set forth in various publications by my colleagues and me, as well as other surgical mesh scientists, starting in 1998.[4] Ethicon's own employees have testified that they agree with our work, including that lighter weight meshes with larger distance between the mesh fibers will reduce the foreign body response and inflammatory reaction compared to heavier weight meshes with smaller pores. Dr. Axel Arnaud, Ethicon's Medical Affairs Group Director, testified that our lightweight large pore concept is "agreed upon by most of the people involved in the science of meshes…this is the basic science about meshes [and] I certainly will not challenge this."[5]

V. SAME MATERIAL IN ALL TVT PRODUCTS

Ethicon has used its "Old Construction" 6 mil Prolene hernia mesh (first marketed in 1974) in all of its TVT meshes since the original TVT was launched in 1998.[6] Axel Arnaud, the Medical Director of Ethicon France acknowledged that the Prolene mesh used in TVT products has never changed.[7] It is my opinion, to a reasonable degree of medical and scientific certainty, that the weight and the distance between the mesh fibers of the "Old Construction" 6 mil Prolene hernia mesh causes a greater FBR and more intense inflammatory response in human tissues than lighter weight meshes with greater distance between the fibers, making the "Old Construction" 6 mil Prolene hernia mesh more susceptible to fibrotic bridging, scar plate formation and encapsulation of the mesh in scar tissue leading to a cascade of harmful reactions in human tissue, including pelvic tissues, thus unnecessarily increasing the risk of injury to women.

In Ethicon's 2013 Clinical Evaluation Report, completed by Ethicon's Medical Affairs Director, Piet Hinoul, he confirms that "All slings are manufactured from Prolene mesh." and are all "made from the same materials…" This report also confirms that while the TVT-S product is a different mode of application, it is the same material.[8]

Because all of Ethicon's TVT line of products, including TVT-R, TVT-O, TVT-A, TVT-E and TVT-S, are made of the same Prolene Old Construction 6 mil mesh, all test results

---

[4] Klosterhalfen, B., Junge, K., Klinge, U. *The lightweight and large porous mesh concept for hernia repair.* Expert Rev. Med. Devices. 2005; 2(1); Klinge U, Klosterhalfen B, Muller M, Ottinger A, Schumpelick V. Shrinking of Polypropylene Mesh in vivo: An Experimental Study in Dogs. Eur J Surg. 1998: 164; 965-969; Klinge, U., Klosterhalfen, B., Birkenhauser, V., Junge, K., Conze, J., Schumpelick, V. Impact of Polymer Pore Size on the Interface Scar Formation in a Rat Model. Journal of Surgiccal Research. 103, 208-214 (2002); Cobb W, Kercher K, Heniford T. The Argument for Lightweight Polyropylene Mesh in Hernia Repair. Surgical Innovation. 2005; 12(1):T1-T7; Cobb WS, Burns JM, Peindl RD, Carbonell AM, Matthews BD, Kercher KW, Heniford BT Textile analysis of heavyweight, mid-weight, and lightweight polypropylene mesh in a porcine ventral hernia model..J Surg Res. 2006 Nov;136(1):1-7. Epub 2006 Sep 22.

[5] Arnaud deposition 9/25/13 772:25 to 777:16; 779:4-11

[6] Holste deposition 7/29/2013 38:21 to 40:15; Batke deposition 08/01/2013 103:11 to104:21

[7] Arnaud deposition 07/19/2013 37:7 to 40:10

[8] ETH.MESH.10150515 Clinical Evaluation Report by Piet Hinoul

performed by Prof. Thomas **Muehl** and published in Otto, et al. regarding the TVT-R device are transferrable and equally applicable to all TVT devices.[9] Therefore, all of my opinions contained in this report are the same as to all of the TVT devices and are discussed in detail in my de bene esse testimony attached as Exhibit "C".

It is my opinion to a reasonable degree of medical and scientific certainty that the entire TVT line of products created and unnecessary risk of patient complications and injuries when implanted in pelvic tissue.

VI. BIOCOMPATIBILITY

A. Foreign Body Reaction

All experimental and clinical studies indicate that surgical mesh products cause an initial and chronic inflammatory tissue response in the patient after implantation. The quality of the inflammatory reaction to foreign bodies of different natures is surprisingly constant, characterized by a rapid accumulation of huge numbers of phagocytic cells, in particular, blood monocytes and tissue-derived macrophages. This type of inflammatory process is known as a foreign body reaction (FBR). It is characterized by an initial inflammatory burst caused by a release of a huge combination of potent inflammatory mediators which then attract other cell types including T-cells, polymorphonuclear granulocytes (PMNs), plasma cells and fibroblasts. Within a few days, this cellular activity forms an early granuloma layer around the mesh fibers recognized by the very typical foreign body giant cells and an outer layer of fibrosis with deposition of collagen. This late stage granuloma is not a static type of chronic inflammation but rather, it represents a chronic wound with an increased cell turnover even years after implantation. The various inflammatory cells, e.g., macrophages, at the interface and in contact with the polymer, undergo apoptotic cell death and are replaced. [Fig. 2]

[9] Klinge, U., Otto, J., and Muehl, T., *High Structural Stability of Textile Implants Prevents Pore Collapse and Preserves Effective Porosity at Strain*, BioMed Research International, vol. 2015, Article ID 953209, 7 pages, 2015. doi:10.1155/2015/953209

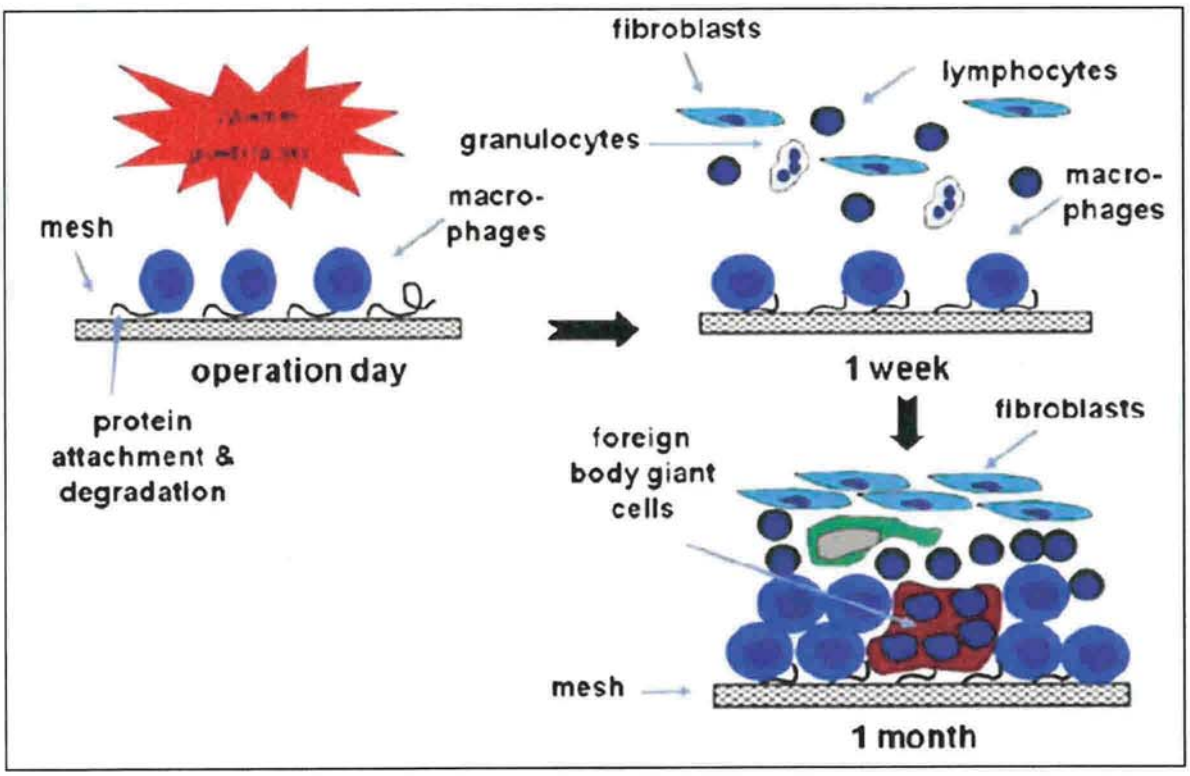


Figure 2[10]

We published our results in 1998 and 1999 of the histological analyses from explanted mesh from both animals and humans. The tissue response in humans was almost identical to the morphological observations in the animal models. In our 1999 study, we reviewed approximately 350 human explant samples of various mesh modifications gathered from centers all over Europe. Even 15 years after explantation, the longest observation in our study, a persistent chronic FBR could still be detected, indicating that mesh is likely never completely inert with respect to local inflammatory processes. The persistence of this FBR is important, especially in younger patients in whom the mesh will remain for several decades. The delay before explantation of mesh for infection of up to 56 months, for chronic pain of up to 48 months and for recurrence of up to 180 months established that in many clinical studies with shorter surveys of less than 1-2 years, the morbidity rates are underestimated.[11,12] It is well known in the medical community that the vagina is considered a "clean-contaminated" field. The implantation of mesh may result in a biofilm which will make it difficult for the host cells to kill the mesh infection; in fact, the development of these biofilms will protect the harmful bacteria that the host cells set out to kill.[13]

---

[10] Semin Immunopathol (2011) 33:235-243 – Formation of a foreign body granuloma at the mesh to host tissue interface

[11] Klinge U, Klosterhalfen B, Muller M, Ottinger A, Schumpelick V. Shrinking of Polypropylene Mesh in vivo: An Experimental Study in Dogs. Eur J Surg. 1998: 164; 965-969

[12] Klinge U, Klosterhalfen B, Muller M, Schumpelick V. Foreign Body reaction to Meshes Used for the Repair of Abdominal Wall Hernias; Eur J Surg 1998; 164: 951–960

[13] Osterberg B. ActaChirScand1979;145:431, Merritt K. J BiomatAppl 1991;5:185, An Y. J Biomed Mater Res (Appl Biomat) 1998;43:338

Furthermore, my colleague and Ethicon's top pathology consultant for 20 years, Bernd Klosterhalfen, informed Ethicon at an expert meeting at Ethicon's Norderstedt facilities in 2006 that based on our studies, the tissues in the body can react to the mesh for up to 20 years.[14]

At another Ethicon expert meeting at Norderstedt the following year, in a PowerPoint presentation to the experts in attendance, Ethicon stated that there can be "excessive FBR > massive scar plate > more shrinkage" depending on the type of mesh.[15] Ethicon stated in that presentation that "small porous meshes (<1mm) lead to 'fibrotic bridging' > increased shrinkage."

Ethicon employees have testified that Ethicon knew before the launch of its pelvic meshes, for both incontinence and prolapse repair, that in some women, there would be a severe FBR and chronic life-altering inflammatory reaction causing debilitating and chronic pain, erosions, recurrence, need for revision surgery and dyspareunia.[16, 17, 18, 19]

It is my opinion to a reasonable degree of medical and scientific certainty that after implantation of the TVT mesh, there is a chronic (permanent) foreign body reaction in a woman's pelvic tissue whereby the woman's body will react to the polypropylene indefinitely, creating a chronic inflammatory response that leads to scarring around the mesh fibers. Claims by Ethicon in its TVT Instructions for Use (IFU) that "a transient foreign body response may occur" and in its TVT marketing brochures that there is "[n]o foreign body reaction after PROLENE mesh implantation" are inconsistent, false and misleading.[20,21] In addition to abundant scientific literature to the contrary, deposition testimony of numerous Ethicon employees in this litigation also demonstrates the falsity of this statement.[22,23, 24]

B. Weight

As is evidenced in countless pages of deposition testimony of Ethicon employees and internal Ethicon documents, Ethicon was aware that lighter weight meshes with greater distance between the mesh fibers lessened the risk of these harmful tissue reactions and thus, lessened the risk of injury to patients.

Ethicon's Medical Affairs Director, Piet Hinoul, recounts the history of Ethicon's attempts to develop lighter weight, larger pore meshes and the multiple reasons for doing so in a 2012 Clinical Expert Report for their light weight, large pore mesh, Ultrapro/Prolift + M:[25]

> Knitted, polypropylene mesh as a reinforcement for Hernia Repair has been used for 40+ years and is an accepted method for reducing recurrence of abdominal wall defects seen in both incisional and inguinal hernias. However,

---

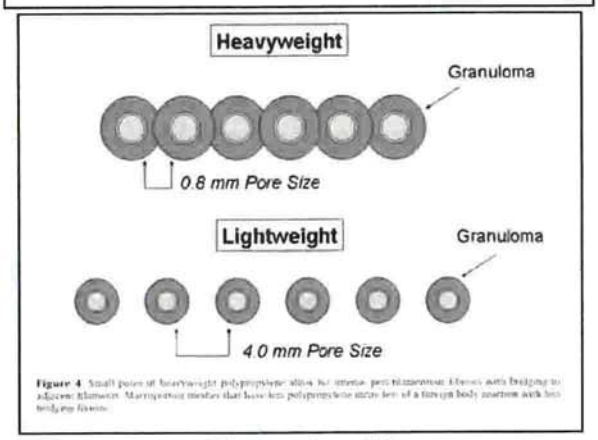
[14] ETH.MESH.00870466 2006 Expert Meeting Norderstedt
[15] ETH.MESH.01782867 "Factors Related to Mesh Shrinkage" Powerpoint presentation by Kestin Spychaj
[16] Hinoul deposition 4/5/12 99:09-99:25, 4/6/12 518:14-520:20, 6/26/13 175:1-176:17, 184:18-22 328:10-24;
[17] Owens deposition 9/12/2012 98:11to 99:07;
[18] Batke deposition 08/01/13 257:23 to 259:13
[19] Arnaud deposition 9/25/13 769:23 to 770:4
[20] ETH.MESH.00339437-442 "5 Years of Proven Performance" Feb 2002
[21] ETH.MESH.02340504 TVT IFU
[22] Barbolt deposition 10/9/13 137:01 to 137:17;
[23] Holste deposition 07/29/13, 51:3 to 53:6
[24] Hellhammer deposition 9/11/2013, 60:24-61:1; 210:15-211:16
[25] ETH.MESH.08315779 "Clinical Expert Report" dtd 9-25-2012 at 782.

implantation of polypropylene mesh is associated with an increase in problems associated with the foreign material implant. Complications associated with these materials have led to changes in implant materials and construction with a goal to 1) reduce implant mass and 2) increase the mesh pore size. The impact of such reductions in material mass on the durability of the repair must be considered. Assessing the breaking strength of healthy tissue, in vivo measurements of maximum pressure during the stresses of coughing, jumping and Valsalva maneuver, and mathematical modeling of abdominal wall forces, have led to the conclusion that synthetic mesh implants, even the lower mass mesh implants, are significantly stronger than required (Deprest et 2006, Cobb et al. 2005).[26]

The Cobb 2005 article states that heavy weight meshes with less than 1 mm between the mesh fibers lead to scarring across the mesh fibers ("fibrotic bridging"). He lists several meshes of varying weights in the article of which Prolene is one of the heaviest weight meshes. [See Figures 3 and 4][27]

Table 1. Polypropylene meshes of differing densities

Surgipro[a]	110 g/m^2
Prolene[b]	105 g/m^2
Marlex[c]	95 g/m^2
Prolite[d]	90 g/m^2
Prolene Soft Mesh[b]	45 g/m^2
Vypro II[b]	35 g/m^2
Ultrapro[b]	28 g/m^2



Figures 3 and 4

[26] ETH.MESH.08315779 "Clinical Expert Report" dtd 9-25-2012 at 782.
[27] Cobb W, Kercher K, Heniford T. The Argument for Lightweight Polypropylene Mesh in Hernia Repair. Surgical Innovation. 2005; 12(1):T1-T7

It is my opinion, to a reasonable degree of medical and scientific certainty, that the greater the surface area of a medical implant, the greater the foreign body reaction and the inflammatory response will be. Ethicon had critical mesh design information regarding the negative consequences in the human tissue of heavy weight, small pore meshes beginning as early as 1998. The heavy weight Prolene mesh (105-110 g/m2) in Ethicon's TVT products is many times stronger than it needs to be for its intended purpose of treating stress urinary incontinence and thus, it is "overengineered" and leaves much more polymer material in a woman's delicate and sensitive pelvic tissues than is necessary. Any pelvic mesh designed with this much excess surface area and weight unreasonably and unnecessarily increases the risk of injury to the patient and is a less safe design than lighter weight mesh as it causes an unnecessarily increased FBR and inflammatory response.

C. Pore Size

Polypropylene filaments cause an intense inflammatory response in the abdominal wall as well as in the tissues of the pelvic floor. There is an increased fibrotic reaction hindering the physiological remodeling at the tissue/implant interface. This intense scar formation contributes to the wound contraction.[28]

In our studies from the late 1990's, in which we evaluated the inflammatory response and fibrotic reaction in the tissues at the interface with the mesh implant, we saw that that large pore mesh (Vypro) was integrated into a loose network of perifilamentous fibrosis with fat tissue present in between the fibers. In contrast, the small pore mesh was incorporated entirely in perifilamentary granulomas and scar tissue, which bridged the whole pore diameter <1 mm. This phenomenon, known as "fibrotic bridging", exists when granulomas, side by side, form a common outer fibrotic capsule joining each mesh fiber and forming a rigid "scar plate" covering the whole mesh. This scar plate leaves no space for further tissue ingrowth and leads to a number of complications including loss of elasticity and pain associated with the rigidity, shrinkage or contraction of the mesh, mesh erosion, nerve entrapment, chronic pain and dyspareunia.

The concept of fibrotic bridging and harmful scar plate formation is evident in numerous internal Ethicon documents. [29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41] [Figure 5]

---

[28] Junge K., Binnebosel, M., Rosch R., Jansen, M., Kammer,, D., Otto, J., Schumpelick, V., Klinge, U., *Adhesion formation of a polyvinylidenflouride/polypropylene mesh for intra-abdominal placement in a rodent animal model*. (2009) Surg Endosc; 23(2):327-33

[29] ETH.MESH.04037600 Innovations in mesh development

[30] ETH.MESH.05920616 7/20/07; Chomiak, Martin to Batke, Boris; Jamieson, Gillian; Koehler, Petra; Hellhammer, Dr. Brigitte SUBJECT: Defining light weight mesh

[31] ETH.MESH.05585033

[32] ETH.MESH.05446127 3/13/2006 Holste, Dr. Joerg to Engel, Dr. Dieter; Manley, Quentin; Storch, Mark L. SUBJECT: AW: Mesh and Tissue Contraction in Animal

[33] ETH.MESH.05475773

[34] ETH.MESH.04015102 3/01/12 Batke, Boris to Mayes, Casey SUBJECT: AW: AGES Pelvic Floor Conference-Gala Dinner Invitation

[35] ETH.MESH.04037600 Mesh Innovations PowerPoint

[36] ETH.MESH.09651393 Invention Disclosure

[37] ETH.MESH.05585066 "Ultrapro" Powerpoint presentation by Boris Batke

[38] ETH.MESH.05916450 "Chronic Pain Prevention/future – Bioengineer's point of view"

[39] ETH.MESH.04037600 "Innovations in Mesh Development" PowerPoint presentation by Boris Batke

[40] ETH.MESH.00237968 "R&D Perspective – The Journey from Prolift to Prolift +M" PowePoint presentation by Cliff Volpe

[41] ETH.MESH.01782867 "Factors Related to Mesh Shrinkage" by Kerstin Spychaj

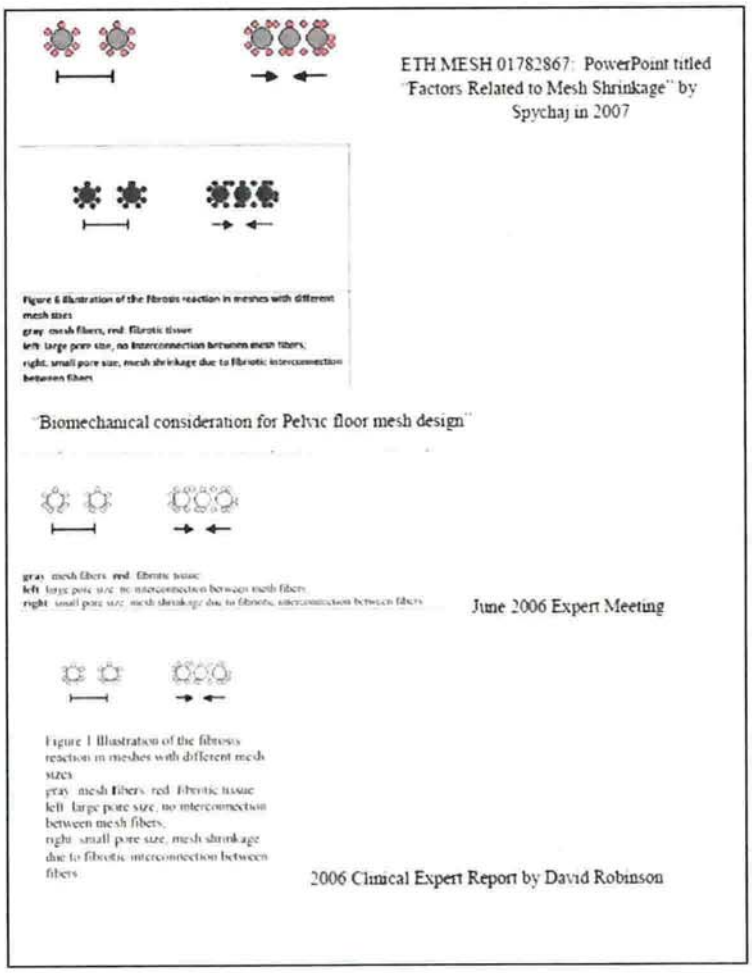


Figure 5

With the development of Vypro, we were able to increase the distance between the mesh fibers by up to 500-600% (Vypro 3-5 mm vs. Prolene <1mm) and decreased the weight from 105-110 g/m^2 (Prolene) to 25g/m^2 (Vypro). Given that the risk of bridging fibrosis is increased by less distance between the fibers, any mesh designed with smaller pores unnecessarily increases the risk of injury to the patient and is a less safe design than mesh a larger distance between the fibers. Simply put: the greater the pore size or open space in between fibers, the less the risk of fibrotic bridging and formation of a rigid and potentially dangerous scar plate encapsulating the mesh. Again, Ethicon had this critical mesh design information regarding the consequences in the human tissue of heavy weight, small pore meshes as a result of our university's cooperative safe mesh design research with them in the 1990's. This is evident in numerous depositions of Ethicon scientists.[42, 43, 44, 45, 46][Figure 6]

[42] Batke deposition 08/01/012 113:3 to 114:3, 172:6 to 174:15, 118:10 to 120:25
[43] Hellhammer deposition 09/12/13 403:18 to 404:9; 407:13-23
[44] Holste depositions 07/29/13 51:3 to 53:6; Holste Deposition 12/14/12 89:20 to90:21
[45] Semin Immunopathol (2011) 33:235–243 - a Scar net formation following large pore (~3 mm) and b scar plate formation following small-pore (~0.3 mm) mesh implantation
[46] Arnaud deposition 9/25/13 756:9 to 757:8

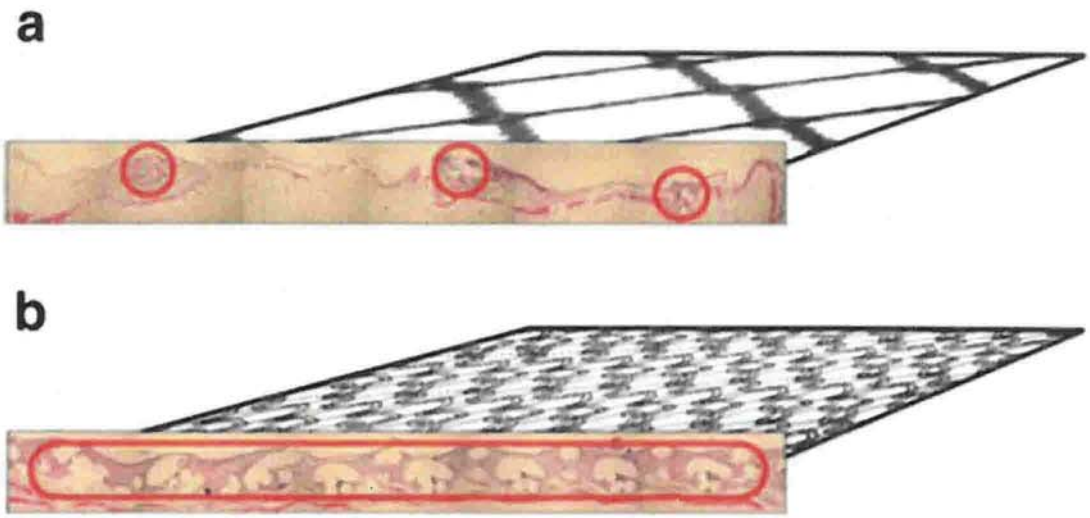


Figure 6

A rather infamous DVD produced by Ethicon and featuring an Ethicon consultant and fellow hernia surgeon, Dr. Todd Heniford, was shown at conferences and seminars in the late 2000's. Ethicon was involved in the production of that DVD as evidenced by the cover of the DVD and their name at the end of it.[47] That DVD touts the benefits of lightweight, large pore meshes and, importantly, describes the dangers of heavy weight, small pore meshes.[48] Dr. Heniford uses slides in the DVD that are from his published literature with his colleague, Dr. William Cobb that has been referenced in numerous Ethicon documents, PowerPoint presentations, professional education materials, expert meetings and Clinical Expert Reports.[49, 50, 51, 52]

At one point in the DVD, published with an Ethicon/JNJ logo from 2007, Dr. Heniford states that with the advent of lightweight, large pore meshes "there really is not a reason to use heavyweight polypropylene in the human body…to say well this is the mesh I've always used is not an excuse to continue to use it." ". Ethicon internal documents by Joerg Holste and Boris Batke indicate Ethicon's awareness of this DVD and its concern that Prolene is very similar to the Marlex shown in the DVD.[53, 54]

In the work of Dr. Cobb, the weight of TVT Prolene is listed as one of the heaviest weighted mesh. Ethicon cites to this work repeatedly. The Prolene mesh in TVT is Ethicon's oldest, heaviest weight, smallest pore polypropylene mesh; yet to this day, Ethicon continues to sell it in all of their currently-marketed TVT products. Although Ethicon now claims that the Prolene

---

[47] B. Todd Heniford 2007 "The benefits of lightweight meshes in Ventral Hernia Repair in Ventral Hernia Repair" Cover
[48] B. Todd Heniford 2007 "The benefits of lightweight meshes in Ventral Hernia Repair in Ventral Hernia Repair" Video
[49] ETH-47802 Cobb WS, Burns JM, Peindl RD, Carbonell AM, Matthews BD, Kercher KW, Heniford BT *Textile analysis of heavyweight, mid-weight, and lightweight polypropylene mesh in a porcine ventral hernia model*.J Surg Res. 2006 Nov;136(1):1-7. Epub 2006 Sep 22.;
[50] ETH.MESH.01424029 Cobb W, Kercher K, Heniford T. *The Argument for Lightweight Polyropylene Mesh in Hernia Repair*. Surgical Innovation. 2005; 12(1):T1-T7;
[51] ETH.MESH.08315779 Piet Hinoul Clinical Expert Report Gynecare Prolift +M Pelvic Floor Repair;
[52] ETH.MESH.00237968 "R&D Perspective - The Journey from Prolift to Prolift +M" Powerpoint by Cliff Volpe
[53] ETH.MESH.05479411 Heavyweight to Lightweight Meshes PowerPoint
[54] ETH.MESH.05918776 2004 email re Marlex Experience

mesh in the TVT is "lightweight", it is clear from the testimony from one of their lead scientists that the mesh is heavyweight.[55] In their depositions, Ethicon employees have acknowledged that they knew that the heavy weight, small pore mesh in TVT Prolene mesh can lead to an increased risk of a greater FBR, more intense and chronic inflammatory response, shrinkage or contraction of the mesh, nerve entrapment in the pelvic tissues, erosions and chronic pelvic pain.[56, 57, 58]

A number of Ethicon employees have testified that they became aware of the lightweight large pore concept by 1998 through Ethicon's collaboration with both Dr. Bernd Klosterhalfen and me during the development of Vypro.[61] Numerous Ethicon internal documents demonstrate the Ethicon was acutely aware of the heavyweight, small pore problem. [62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73,74] Ethicon employees have also admitted that the Prolene mesh used in TVT products was heavyweight and small pore mesh. [75, 76]

A decision was apparently made in 1998 to change the TVT Prolene mesh construction. In 1998, Ethicon indicated that its "long-term desire [was] to support the PHS [Prolene Hernia System] and TVT devices with **the new construction material**."[77] [Emphasis added] Ethicon seemingly planned from the time of the launch of TVT to replace the "Old Construction 6 mil" mesh with a new mesh construction; however, they delayed making these improvements as stated below:

> Product's improvements
>
> **In order to meet our objective and launch TVT on October 30th, 1997, we decided to simplify our activity both at manufacturing and development level.**
>
> As we have moved ahead in our European activity, we have in fact realised that product improvement is not a major issue in Europe.
>
> **Anyhow, we recognise that some amendments are desirable and therefore are going to work on a second generation product to be released 1 Q99.**
>
> **Following changes will be made:**
>
> **• new construction Prolene* mesh to be used (after clinical test by Prof. Ulmsten and Prof. Nilsson** - 40 patients with 6 moths follow-up)

[55] Hellhammer deposition 09/11/13 156:15-23
[56] Batke deposition 08/01/13 87:12 to 88:10, 113:3 to 114:3, 257:23 to 259:13
[57] Holste deposition 07/29/13 51:3 to 53:6, 55:22 to 57:4
[58] Vailhe deposition 6/20/13 182:2 to 185:5
[61] Batke deposition 08/01/12, 113:3 to 114:3, 172:6 to 174:15, 118:10 to 120:25; Hellhammer deposition 09/11/13 57:16 to 59:16; Hellhammer deposition 09/12/13 550:1 to550:14; Holste depositions 07/29/13, 51:3 to 53:6; Holste Deposition 12/14/12, 89:20-90:21; Arnaud deposition 09/25/13 756:9 to 756:19
[62] ETH.MESH.04037600 Innovations in mesh development ETH.MESH.01782867 "Factors Related to Mesh Shrinkage" by Kerstin Spychaj
[63] ETH.MESH.05920616 7/20/07; Chomiak, Martin to Batke, Boris; Jamieson, Gillian; Koehler, Petra; Hellhammer, Dr. Brigitte SUBJECT: Defining light weight mesh
[64] ETH.MESH.05585033
[65] ETH.MESH.05446127 3/13/2006 Holste, Dr. Joerg to Engel, Dr. Dieter; Manley, Quentin; Storch, Mark L. SUBJECT: AW: Mesh and Tissue Contraction in Animal
[66] ETH.MESH.05475773
[67] ETH.MESH.04015102 3/01/12 Batke, Boris to Mayes, Casey SUBJECT: AW: AGES Pelvic Floor Conference-Gala Dinner Invitation
[68] ETH.MESH.04037600 Mesh Innovations PowerPoint
[69] ETH.MESH.09651393 Invention Disclosure;
[70] ETH.MESH.05585066 "Ultrapro" Powerpoint presentation by Boris Batke;
[71] ETH.MESH.05916450 "Chronic Pain Prevention/future – Bioengineer's point of view"
[72] ETH.MESH.04037600 "Innovations in Mesh Development" PowerPoint presentation by Boris Batke;
[73] ETH.MESH.00237968 "R&D Perspective – The Journey from Prolift to Prolift +M" PowePoint presentation by Cliff Volpe;
[74] ETH.MESH.01203957 The Future of surgical meshes: the industry's perspective PowerPoint by Piet Hinoul
[75] Hellhammer deposition 09/12/13 550:1-14
[76] ETH.MESH.05479535
[77] ETH.MESH.09264884

- 5 mm needles instead of 6 mm (width)
- shiny surface of needles (instead of opaque) to provide "slim" effect
- new shrinking tube (transparent) for needle-tape swaging
- blister pack

Manufacturing and operations will be followed up during 1998, so as to ensure release of second generation product 1 Q99.[78] [Emphasis added]

Unfortunately for patients, Ethicon chose not to replace its "Old Construction 6 mil" Prolene mesh in its TVT products but rather, chose to use the same mesh they had been marketing since 1974, without regard to critical design developments and considerations that they had studied, developed and were ready to launch.

It is my opinion, to a reasonable degree of medical and scientific certainty that the smaller the distance between the fibers of a mesh implant, the greater the risk of scar tissue forming in the pores ("bridging fibrosis" or "fibrotic bridging"). As early as 1998, and certainly by the early 2000's, Ethicon had critical design information that the risk of bridging fibrosis is increased by surgical mesh with pore size less than 1mm in all directions, which in turn increases the risk of a rigid scar plate forming throughout the mesh, leading to integration of the entire mesh in scar tissue. Any pelvic mesh designed with pores this small unreasonably and unnecessarily increases the risk of injury to the patient and is a less safe design than mesh with greater distance between the fibers.

It is also my opinion, to a reasonable degree of medical and scientific certainty, that Ethicon's failure to implement new, critical mesh design changes (lighter weight, larger distance between the fibers) in its TVT products before its launch in 1998 was unreasonable, compromised patient safety and has led to patient complications like chronic inflammatory reaction, excessive scarring through and around the mesh, nerve entrapment, chronic pain, dyspareunia, erosions, recurrence and the necessity of reoperation in an attempt to correct these problems. The Prolene mesh in Ethicon's TVT products is unsuitable for use as a permanent implant for treatment of a woman's stress urinary incontinence.

D. Pore Deformation

In approximately 2005, I applied for and received a grant to study the porosity of textile meshes in an attempt to objectify porosity in a reproducible manner. Working with an engineer at the FH Aachen University of Applied Sciences, Prof Thomas Muehl, we published the results of this granted project in 2008 in the Journal of Biomedical Materials Research Part B: Applied Biomaterials.[79]

Our research was based on my research since the late 1990's that pore sizes that prevent fibrotic bridging and will permit ingrowth of physiological tissues should exceed 1 mm between two polypropylene filaments. As stated in our publication, "To exclude large pore areas that may be provided by long and thin pores with narrow parts of pores, the pore geometry has to be

[78] ETH.MESH.10183005

[79] Muehl T, Binnebosel M, Klinge U, Goedderz T. New Objective Measurement to Characterize the Porosity of Textile Implants. J Biomed Mater Res Part B: Appl Biomater. 2007; 84B:176-183

evaluated as well. Therefore, only those pores and those parts of the pores are extracted, which have dimensions greater than 1mm or 1000 µm in all directions. The remaining porosity is defined as 'effective porosity'".

We published two additional studies of the pore size/porosity of surgical meshes in 2013 and 2014 based on our 2008 work which studied and analyzed Ethicon's Prolift and Prolift +M pelvic organ prolapse meshes. [80] [81]

An Ethicon R&D Scientist, Vincenza Zaddem, Team Leader of Prolift +M and Technical Lead of Prolift, was shown the Muehl study from 2007 and she testified that it sounded like a valid test and that she believed that it would be a good test for Ethicon to look into in order to determine the effective porosity and effective porosity under strain of their pelvic meshes.[82] This was again confirmed in testimony by another Ethicon employee, Joerg Holste and circulated numerous times within Ethicon as a "more sophisticated set up" than Ethicon's method of porosity testing. [83, 84, 85] Ethicon was also aware of the concept of "effective porosity" and the necessity of maintaining pore sizes of >1mm after stretch.[86, 87, 88, 89, 90, 91] [Figure 7]

[80] J. Otto, et al., Elongation of textile pelvic floor implants under load is related to complete loss of effective porosity, thereby favoring incorporation of scar plates; J Biomed Mater Res A 2013 Apr 29
[81] Klinge, U., Otto, J., Muehl, T. (2014) High Structural Stability of Textile Implants Prevents Pore Collapse and Preserves Effective Porosity at Strain
[82] Zaddem deposition 03/28/12, 387:14 to 387:20
[83] Holste deposition 10/9/2013, 417:9 to 418:22
[84] ETH.MESH.02184130 2008 email circulating New Objective to Characterize the Porosity of Textile Implants
[85] ETH.MESH.04945136 2010 email circulating New Objective to Characterize the Porosity of Textile Implants
[86] ETH.MESH.03021946 T-Pro Stage Gate Meeting on August 25, 2008
[87] ETH.MESH.02587926 When the Implant Worries the Body
[88] ETH.MESH.01752532: Mesh Design Argumentation Issues
[89] ETH.MESH.01785259 January 17, 2010 Email re; +M relaxation
[90] ETH.MESH.02587925 "When the implant worries the body" PowerPoint presentation
[91] ETH.MESH.02185582 "Biomechanical Considerations for Pelvic Floor Mesh"

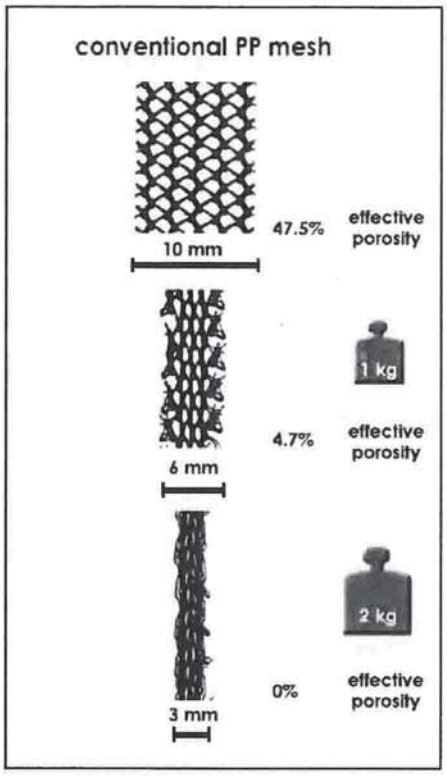


Figure 7[92]

Ethicon estimates that its TVT slings will encounter elongation or stretch once placed in a woman's body up to 50%.[93] In other Ethicon internal documents, Ethicon estimates the in vivo forces placed on its TVT slings will be approximately 1N.[94] In other Ethicon documents, Ethicon scientists quote the intra-abdominal pressures as follows: [95]

- Standing: 23cm H_2O
- Lifting 5kg: 22 cm H_2O
- Valsalva: 79 cm H_2O
- Coughing: 96 cm H_2O
- Bearing down: 102 cm H_2O

Moalli et al. cited our published work in 1999 that "forces applied to mid-urethral slings in vivo is estimated to be in the range of approximately 5 to 15 N or 1.1 to 3.4 lbs." [96]

When developing the protocol for testing the TVT meshes, I determined the uniaxial forces that would be placed on the mesh using the following assumptions:

---

[92] ETH.MESH.03021946 T-Pro Stage Gate Meeting 8/25/08
[93] ETH.MESH.00541379 Memo to File from Martin Weisberg re: Mesh Fraying to TVT Devices; ETH.MESH.00584811
[94] ETH.MESH.00584491 2006 email re AFNOR standards; ETH.MESH.01219414: Elongation Characteristic of Laser Cut PROLENE Mesh for TVT; Smith deposition 08/21/2013, 587:22 to 588:23
[95] ETH.MESH.05237872 "Mesh Properties – How important are they?" by Peter Meier
[96] Moalli P., Papas, N., Menefee S., Albo, M., Meyn, L., Abramowitch, D., Tensile properties of five commonly used mid-urethral slings relative to TVT *Int Urogynecol J* (2008) 19:665-633

· In contrast to flat meshes without tensile stress, narrow slings may be considered to work as ligaments having to withstand uniaxial strain.[97] This is undisputable for the process of implantation and the early postoperative time. To mimic the mechanical strain in this phase, we applied strain to the mesh in an uniaxial setting;

· The strain applied should cover the forces and the elongation that can be assumed to be relevant;

· Forces were related to the width of the sling, and thus N/cm was used for comparison with estimated membrane tensions;

· Membrane tension of 16 N/cm was calculated as requirement for the abdominal wall. As the diameter of the pelvis is less than a half of the abdominal wall, the membrane tension should be less than half; [98]

· Experimental studies by DePrest et al resulted in a membrane tension of 2 to 5 N/cm as strain to be expected in the pelvic floor, 1 N/cm in non-prolapsed tissues;

· The tensile strain in the pelvic floor is expected to lead to an elongation of the textile. An elongation of up to 20% is considered to form the comfort zone, and elongation of 40% defines the safety zone; [99]

· The tensile force during implantation procedure of a pelvic mesh is considered to be up to 30 N, [100] and correspondingly, the in vitro simulation should have less tensile strength;

· The intra-abdominal pressure to the pelvis is estimated by Janda to be 8.3 kPa, whereas an intra-abdominal pressure of 20 kPA is estimated to stress the abdominal wall to 16 N/cm - a lower intra-abdominal pressure leads to a lower tensile load. Considering the lower diameter of the pelvis, a mechanical load of less than 10 N/cm would be reasonable; [101]

· Pullout force is considered by Ethicon to be 1.6 N/cm (20% elongation; 164g = "physiological" load); [102]

As a consequence, although the burst strength of Prolene is 91 N/cm [103] , we applied forces of 1 to 10 N to the slings, which should cover an elongation of less than 50%; altogether, a range that is used in internal studies of Ethicon as well.[104]

---

[97] ETH.MESH.04048515 at 8518: KOL Interview of Carl G. Nilsson
[98] ETH.MESH.02010834 "Biomechanical consideration for Pelvic floor mesh design" by Juergen Trzewik and Christoph Vailhe; ETH.MESH.04048515 Nilsson KOL interview; Trzewik deposition 09/18/2013 226:20-22; ETH.MESH.02227224 Thunder PowerPoint 05/09/2008
[99] ETH.MESH.02010834 "Biomechanical consideration for Pelvic floor mesh design" by Juergen Trzewik and Christoph Vailhe
[100] ETH.MESH.02588182
[101] ETH.MESH.04006021; ETH.MESH.02185596
[102] ETH.MESH.03658927
[103] Klosterhalfen B, Klinge U, Schumpelick V.; Functional and morphological evaluation of different polypropylene-mesh modifications for abdominal wall repair. Biomaterials (Dec 1998) 19(24):2235-46
[104] Moalli P, Papas N, Menefee S, Albo M, Meyn L, Abramowitch D; Tensile properties of five commonly used mid-urethral slings relative to TVT. Int Urogynecol J (2008) 19:655-663

Ethicon's biomechanical engineer, Juergen Trzewik's "Invention Disclosure" helped to further define our porosity testing parameters and protocols. [105] In his Invention Disclosure, Dr. Trzewik wrote:

> The physiological, mechanical boundary conditions can be separated into two main conditions. The comfort zone is defined by the load situation within the implant under normal physiological conditions.
>
> **Here, 'the main load of 2,5 kPa is delivered by the weight of internal organs 2,5 kPa**
>
> *[1] S.Janda,"Biomechanics of the pelvic floor musculature."TU Delft, 2006.[2] K.K.O'Dell, A.N.Morse, S.L.Crawford, and A.Howard,"Vaginal pressure during lifting, floor exercises, jogging, and use of hydraulic exercise machines," Int. Urogynecol. J. Pelvic. Floor. Dysfunct., vol. 18, no. 12, pp. 1481-1489, Dec.2007.*
>
> **The material of the implant basic structure is designed to be characterized by a comfort zone of high elasticity at a low physiological load and a safety zone characterized by low elasticity at high loads. Both zones are separated by the construction of the yield point by tangential approximation of the stress strain curve for the zone of initial elongation and the slope of region of high stress. The yield point for vaginal tissue is considered to be between 10%-200% of area strain.**
>
> *[1]C.Rubod,M.Boukerrou,M.Brieu,P.Dubois,andM.Cosson,"Biomechanicalpropertiesofvaginaltissue.Part1: new experimental protocol," J. Urol., vol. 178, no. 1, pp. 320-325, July2007.[2]H.Yamada,StrenghtofBiologicalMaterials.Baltimore:TheWiliams&WiliamsCompany,1970.*
>
> **The stretch of vaginal tissue may exceed 300 % under certain conditions.**
>
> *[3]J.M.Miller,D.Perucchini,L.T.Carchidi,J.O.DeLancey,andJ.Ashton-Miller,"Pelvicfloormusclecontractionduringa cough and decreased vesical neck mobility," Obstet. Gynecol., vol. 97, no. 2, pp. 255-260, Feb.2001.*
>
> **The yield point is individually defined for the different structures of the implant (e.g., the arms of the implant are characterized with a lower yield point than the implant body). The material behaviour simulates the behaviour of tendon structures is described by a significantly reduced elasticity compared to the implant body** *.[H. Yamada, Strength of Biological Materials. Baltimore: The Wiliams & Wiliams Company, 1970]* **The yield point for the arms should not exceed 10 %.**
>
> **The implant material is anisotropic and stretches differently in**

[105] ETH.MESH.09651393 Invention Disclosure

longitudinal and transversal direction. The yield point in the transversal direction exceeds the longitudinal direction between 100%-500%.

[1]C.Rubod,M.Boukerrou,M.Brieu,P.Dubois,andM.Cosson,"Biomechanicalpropertiesofvaginaltissue.Part1: new experimental protocol," J. Urol., vol. 178, no. 1, pp.320-325, July2007.[2] H. Yamada, Strength of Biological Materials. Baltimore:The Wiliams & Wiliams Company, 1970.

Biomechanical features like increased flexibility are undesired during the surgical procedure of implant placement, to avoid any uncontrolled or undefined stretching of the implant during implantation. Pre- straining of the implant would change the mechanical properties of the implant. A temporary stress- shielding of the long-term implant is necessary during implantation and wound contraction.

[Y.Abramov,A. R. Webb, J. J. Miller,A. Alshahrour, S. M. Botros,R. P. Goldberg ,G. A. Ameer ,and P .K. Sand ,"Biomechanical characterization of vaginal versus abdominal surgical wound healing in the rabbit,"Am. J. Obstet. Gynecol., vol. 194, no. 5, pp. 1472-1477, May2006]

The yield point of the implant is lower than <10% before absorption of the supporting stress shielding structure.

As a consequence of all this information, we performed measurements to 11 mm TVT and TVT-O slings at a strain of

- 102 g (0.9 N/cm)
- 164 g (1.5 N/cm)
- 250 g (2.2 N/cm)
- 500 g (4.5 N/cm)
- 1000 g (8.9 N/cm)

The significance of the Muehl method of testing these mesh products is that it provides useful data in terms of how a mesh will perform in use, particularly in regard to the risk of fibrotic bridging. The first most important observation from this testing was that the textile porosity, the textile porosity under strain, the effective porosity and the effective porosity under strain in TVT produced results that did not meet the most basic requirements that Ethicon had utilized since the late 1990's, early 2000's. As minimal strain was applied to the test sample, the geometric shape of the pores deformed and ultimately collapsed. This deformation led to even smaller pores that make the Prolene mesh highly susceptible to fibrotic bridging, encapsulation by a rigid scar plate and the array of potential complications that occur as a result of this inflammatory process.

Another significant observation during the porosity testing by Prof. Muehl and me was the "curling", sometimes referred to as "roping", that occurred in the TVT under minimal strain. As

strips of mesh begin to curl, the fibers become situated too close together enhancing the inflammatory response and leading to fibrotic bridging.

Yet another significant observation during the stretch testing in our publications was the "fraying" at the edges of the mesh which could be seen upon removal from the package but became markedly worse in the TVT mesh sample at minimal strain, especially in the mechanical cut slings. These frayed edges create an increased inflammatory process and increase the tendency for curling. As fraying occurs, mesh particles can be released into the tissue, increasing the local load with foreign body surfaces, and creating an even greater inflammatory response in the tissues. This will be discussed in more detail below in this report.

After being subjected to even minimal strain or tension, the TVT slings, frayed and demonstrated deformation of the pores; they also failed to return to their original or near-original geometric shape and design. This phenomenon of permanent elongation "is mostly due to a rearranging of the sling's architecture and should not be confused with the traditional mechanics definition of plastic deformation of an elastic material."[106] It is my opinion, to a reasonable degree of medical and scientific certainty, that this permanent elongation of TVT slings leads to permanent pore deformation or collapse and increases the risk of an enhanced inflammatory reaction in the human tissues and thus increases the risk of excessive scarring and the cascade of events related to an enhanced and chronic inflammatory response. It was determined in 2009 by Ethicon that Prolene mesh in its TVT products would distort irreversibly at 164 grams of force.[107, 108] This irreversible damage would lead to the series of events that are known to occur with permanent distortion or deformation.

Ethicon's biomechancial engineer, Juergen Trzewik, proposed various ideas to prevent pore collapse in Ethicon's pelvic floor meshes; however, Ethicon never utilized these or other design changes to reduce the risk of pore collapse and deformation in its TVT meshes. [Figure 8 and 9]

---

[106] Moalli P., Papas, N., Menefee S., Albo, M., Meyn, L., Abramowitch, D., *Tensile properties of five commonly used mid- urethral slings relative to TVT.* Int Urogynecol J (2008) 19:665-633

[107] ETH.MESH.00345806 2009 email re Preclin

[108] ETH.MESH.00072085 Final Report PSE Accession Number 05-0396 Project Number 67379

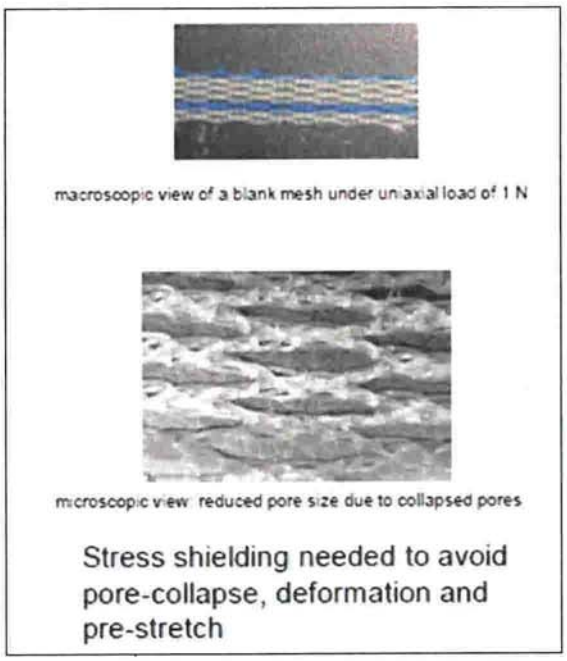


Figure 8[109]

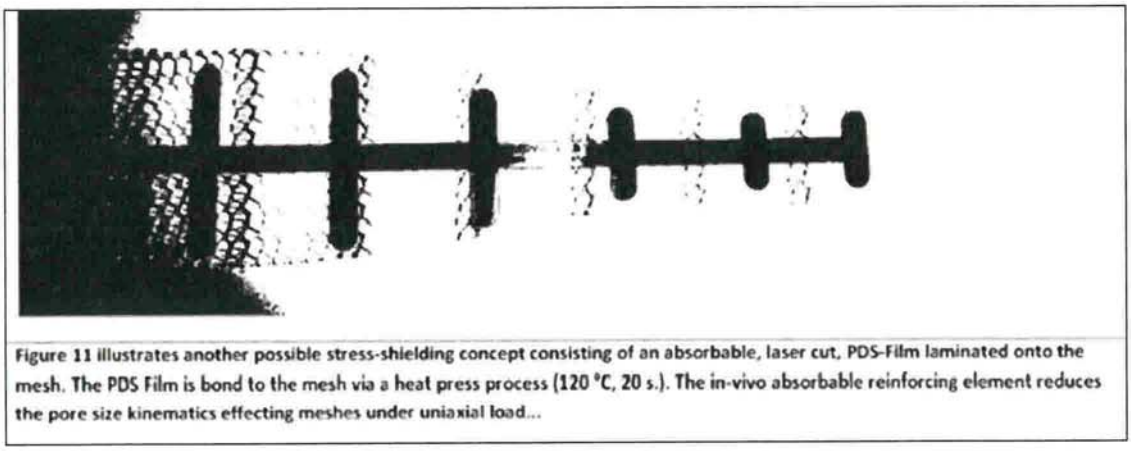


Figure 9[110]

In a 2006 email discussing new French AFNOR standards for surgical mesh testing, a Senior Scientist at Ethicon, Gene Kammerer, while referencing the an article by Lin, et al., stated that "the article shows the maximum forces applied to the sling under the urethra is about 1N or 100 grams. So, for in vivo function (while the mesh is in the body) a force to elongate should correspond to about 1N"[111], which is in sharp opposition to the tensile forces withstood by the Prolene hernia mesh.

[109] ETH.MESH.02227224 MGPP Thunder Decision Meeting PowerPoint presentation
[110] ETH.MESH.02010849
[111] ETH.MESH.00584491 2006 email re AFNOR standards

In testing by Moalli et al. of the Ethicon TVT slings, they found in uniaxial testing that "the permanent elongation after C1 (ten cycles between 0.5 and 5 N or roughly 0.1 and 1.1 lbs.) of the Gynecare mesh was different from that of all the other samples tested. Gynecare samples permanently elongated by 17.5 +/- 4.2%, indicating that although very little force is applied, there is irreversible deformation of the TVT." The study authors went on to state:

> The most important finding of the paper is that Gynecare TVT mesh has a unique tensile behavior which is characterized by an initial region of very low stiffness in which the mesh easily elongates in response to small changes in force…As a result of this behavior, after cyclical loading at low loads…Gynecare mesh permanently elongated by more than 10% of its initial length, **confirming the easy permanent deformability of this mesh that is observed clinically during placement.**" (emphasis added)

The published testing by Moali, et al. of the TVT mesh is virtually identical in set up and results as our published testing of the TVT mesh. [Fig. 10 and 11)

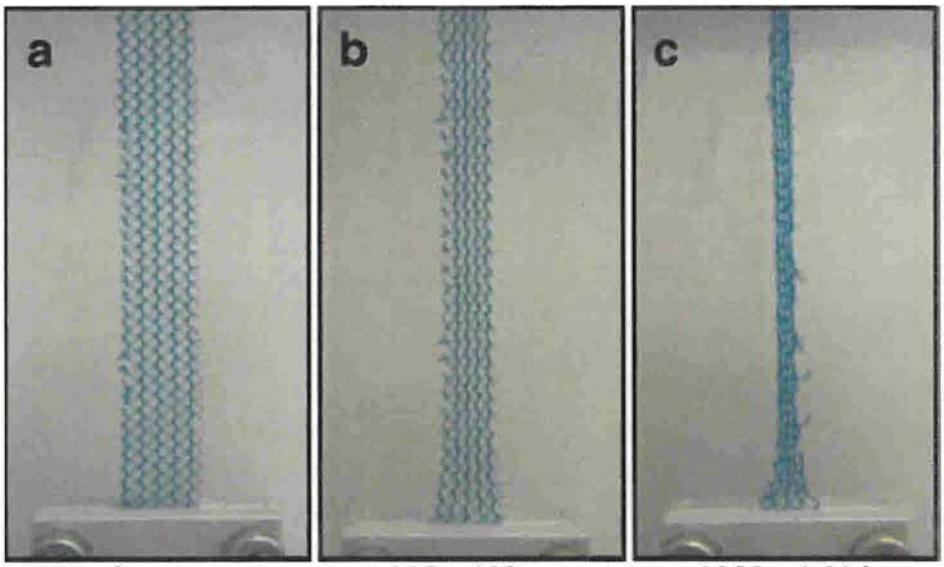


Figure 10[112]

[112] Moalli P, Papas N, Menefee S, Albo M, Meyn L, Abramowitch D; Tensile properties of five commonly used mid-urethral slings relative to TVT. Int Urogynecol J (2008) 19:655-663

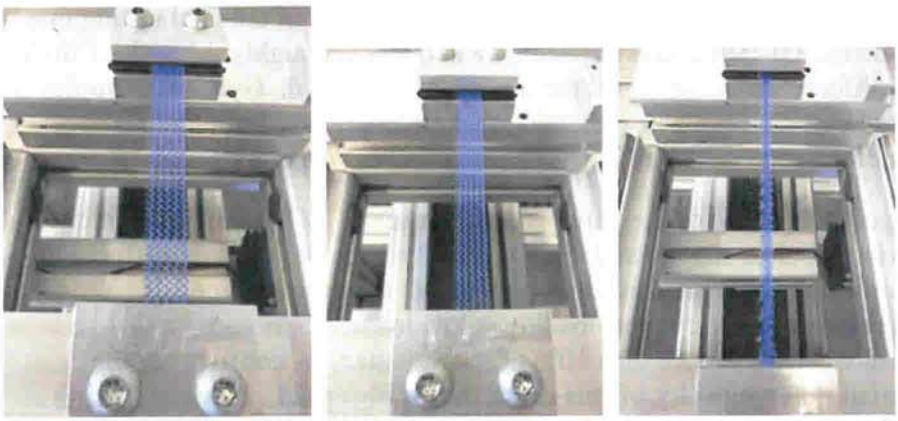


Figure 11[113]

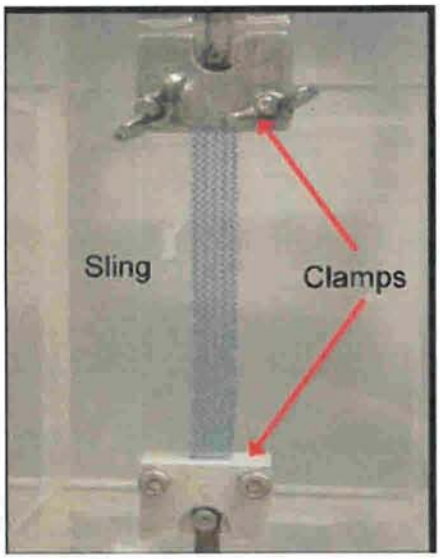
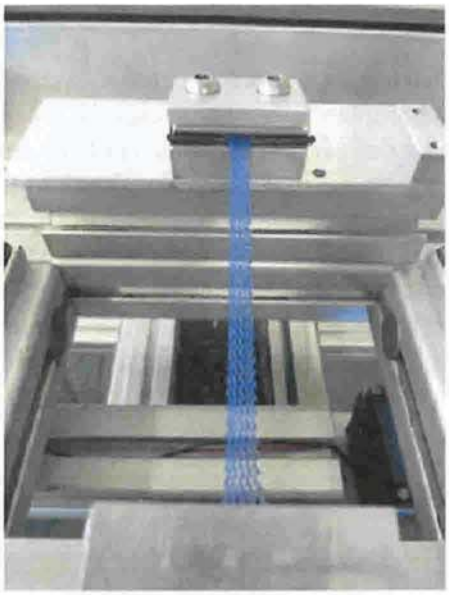


Figure 12[114]

[113] Images from the Expert report of Prof. Dr.-Ing Thomas Muehl
[114] Moalli P, Papas N, Menefee S, Albo M, Meyn L, Abramowitch D; Tensile properties of five commonly used mid-urethral slings relative to TVT. Int Urogynecol J (2008) 19:655-663



1000 g → 8.92 N/cm

Figure 13[115]

In his recent deposition, the Medical Director of Ethicon France, Axel Arnaud, states: "My understanding of this is there are two – normally two types of pores [in the TVT Prolene mesh], and when you pull on them, their size might change." He also agrees that when tension is placed on the mesh that the pore sizes change.[116] Both Dr. Arnaud and another Ethicon Medical Director, Piet Hinoul have testified in this litigation that they respect my work and the work of my colleagues, including Dr. Klosterhalfen, and testified that we are highly qualified in this very specific field of biomaterials research on surgical meshes. In fact, Dr. Hinoul testified that he would defer to me as to whether the pores in Ethicon's meshes collapse and deform under load and further stated that if Ethicon's pelvic floor meshes do collapse and deform making them, in essence, microporous meshes, "Ethicon would not have wanted to sell that mesh." [117,118,119]

My opinion, to a reasonable degree of medical and scientific certainty is that a knitted surgical mesh device like the TVT that is permanently implanted in human tissue must be designed in such a manner that the pores of the mesh do not collapse and deform upon the expected forces of implantation as well as the expected in vivo forces. Under minimal strain, the TVT mesh pores deform and collapse thereby increasing the risk of injury to patients in which it is implanted and is a less safe design than products that better withstand these conditions and do not display these poor outcomes. Permanent deformation and pore collapse of the TVT mesh leads to fibrotic bridging, scar plate formation, excessive scarring through and around the mesh and a host of tissue complications that can lead to chronic pain, recurrence, erosions, dyspareunia and need for reoperation, to name a few, making it unsafe for its intended purpose of being permanently implanted in a woman's pelvic tissue.

---

[115] Images from Expert Report of Prof. Dr.-Ing. Thomas Muehl
[116] Arnaud deposition 07/19/2013 108:17 to 109:11
[117] Hinoul trial 01/1616 1112:17 to 1114:4
[118] Hinoul deposition 09/19/12 1054:9 to 1055:5; 1063:5 to 1065:11
[119] Arnuad deposition 11/16/12 370:9 to 371:13; 373:20 to 375:2

E. Mesh Contraction

Mesh contraction, also known as mesh shrinkage, retraction, bunching or wrinkling, is a common phenomenon after mesh implantation that is closely related to scarring and fibrotic bridging. Mesh contraction can be defined by a reduction of the surface area of the original implanted mesh. The surface reduction is due not to shrinkage of the mesh fibers themselves but rather to a retraction of the fibrotic scar tissues around the mesh. Retraction of the mesh implant is a physiologic reaction of maturing scar that is characterized by a constant water loss and, consequently, a subsequent surface area decrease to an average of 60% of the former wound region. It is known to take place in the first few weeks after implantation but can last as long as 12 months or more after surgery. The medical literature and Ethicon's own internal documents report that there is considerable mesh contraction of surgical meshes made of polypropylene. [120, 121, 122, 123, 124, 125, 126]

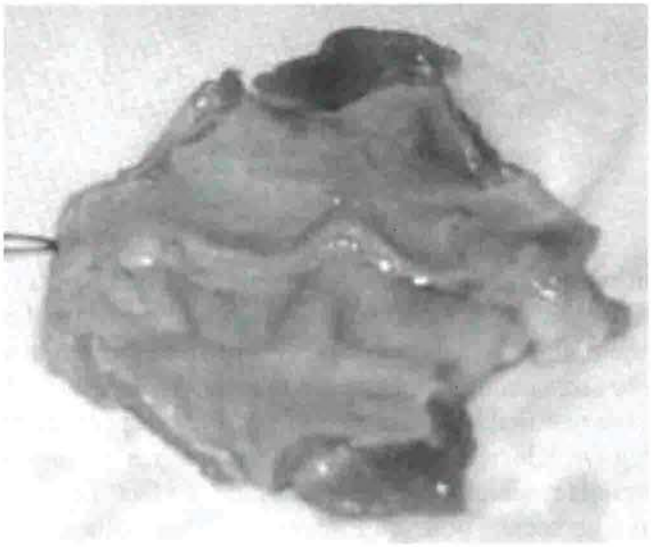


Figure 14[127]

[120] ETH-47802 Cobb WS, Burns JM, Peindl RD, Carbonell AM, Matthews BD, Kercher KW, Heniford BT Textile analysis of heavyweight, mid-weight, and lightweight polypropylene mesh in a porcine ventral hernia model..J Surg Res. 2006 Nov;136(1):1-7. Epub 2006 Sep 22.

[121] Cobb W, Kercher K, Heniford T. The Argument for Lightweight Polyropylene Mesh in Hernia Repair. Surgical Innovation. 2005; 12(1):T1-T7

[122] Tunn R, Picot A, Marschke J, Gauruder-Burmester A, Sonomorphological evaluation of polypropylene mesh implants after vaginal mesh repair in women with cystocele or rectocele. Ultrasound Obstet Gynecol. 2007 Apr;29(4):449-52.

[123] ETH.MESH.01192895 Velemir L, Amblard J, Fatton B, Savary D, Jacquetin B, Transvaginal mesh repair of anterior and posterior vaginal wall prolapse: a clinical and ultrasonographic study. Ultrasound Obstet Gynecol (2010)

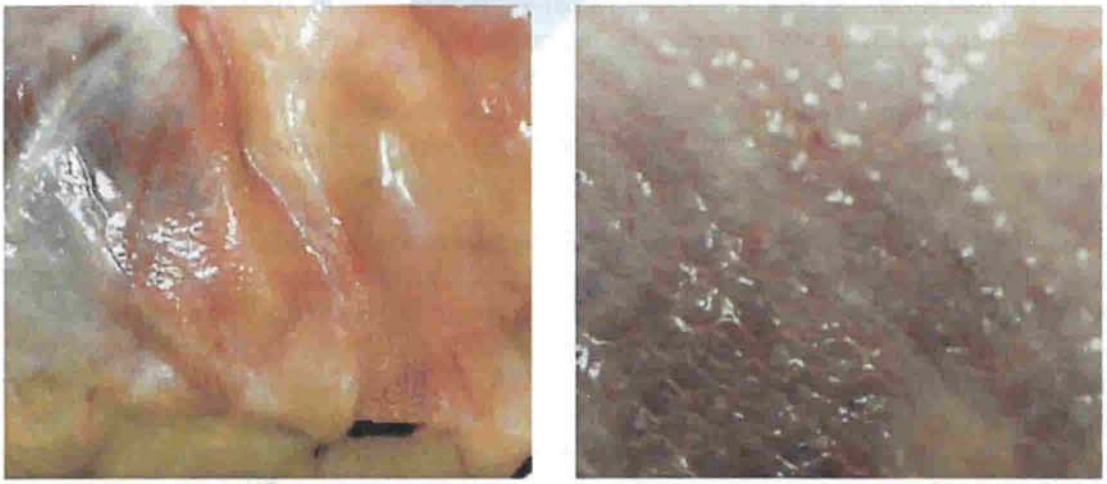
[124] Letouzey V, Fritel X, Pierre F, Courtieu C, Marès P, de Tayrac R. Informing a patient about surgical treatment for pelvic organ prolapse. Gynecol Obstet Fertil. 2010 Apr;38(4):255-60.

[125] Vollebregt A, Troelstra A, van der Vaart C. Bacterial Colonisation of collagen-coated polypropylene vaginal mesh: Are additional intraoperative sterility procedures useful? Int Urogynecol J. 2009; 20:1345-1351

[126] Klinge U, Klosterhalfen B, Muller M, Ottinger A, Schumpelick V. Shrinking of Polypropylene Mesh in vivo: An Experimental Study in Dogs. Eur J Surg. 1998: 164; 965-969

[127] Klinge U, Klosterhalfen B, Muller M, Ottinger A, Schumpelick V. Shrinking of Polypropylene Mesh in vivo: An Experimental Study in Dogs. Eur J Surg. 1998: 164; 965-969

Figure 15[128]



Traditional polypropylene mesh. 90 days post-implantation. Fold development (in-vivo study)

Lightweight VYPRO* II mesh. 90 days post-implantation. Fold-free incorporation (in-vivo study)

Figure 16[129]

While developing its prolapse meshes, the TVM group in 2006 advised Ethicon of the common occurrence of retraction or shrinkage which then creates a "cord-like" mesh.[130] This issue not only leads to poor coverage leading to recurrence, but will also increase locally the amount of foreign body reaction due to pore collapse. This phenomenon then leads to additional complications depending from the location of the mesh including: pain, dyspareunia, nerve

[128] Costello CR, Bachman SL, Ramshaw BJ, Grant SA., Materials characterization of explanted polypropylene hernia meshes. J Biomed Mater Res B Appl Biomater. 2010 Aug;94(2):455-62

[129] Ethicon Products Worldwide – Tissue Reinforcement Solutions 2004

[130] ETH.MESH.01774758 December 2006 email regarding TVM Group mesh design input

entrapment, increased inflammation, urinary and fecal incontinence, urinary retention, blood vessel injury and others.

In referencing his internal Ethicon paper "Shrinking Meshes?", Ethicon scientist Joerg Holste stated in an email on March 13, 2006 "this was our scientific statement on mesh shrinkage: Basically, small pores, heavy weight meshes induce more fibrotic bridging tissue reaction causing more mesh shrinkage during maturing of the collagenous tissue. See my presentation about biocompatibility."[131] That email was in response to a string of internal Ethicon emails in which Ethicon employees were discussing their concerns over a study by Ramshaw in which polypropylene meshes actually shrank more than polyester.[132]

In February of 2007, Dr. Kerstin Spychaj, Ethicon R&D prepared a presentation entitled, "**State of the knowledge in 'mesh shrinkage' – What do we know**?" which she presented at an Ethicon Expert Meeting on February 23, 2007 at Ethicon's Norderstedt facility. Dr. Spychaj did a literature review and concluded that the "ideal mesh" in order to avoid shrinkage would be a lightweight material (partially absorbable) with a pore size > 1mm and mild but not excessive FBR and wound contraction with swift and adequate tissue growth.[133] Not only had Ethicon determined that shrinkage was obviously critical to the quality of its mesh products, they also stated that it could cause "vaginal anatomic distortion which may eventually have a negative impact on sexual function." Furthermore, they stated that "its treatment is difficult."[134] Several other Ethicon employees and/or consultants provided testimony or presentations regarding the issue of mesh shrinkage.[135, 136, 137, 138, 139] The Prolene mesh in TVT is both heavyweight and has pore sizes <1mm in all directions, making it highly susceptible to harmful, painful contraction.

Johnson & Johnson hired an outside consulting firm named PA Consulting in 2010 to do a comprehensive and confidential analysis of its surgical meshes in order to look at the increased risk of erosions in its meshes. The final report was issued in June 2011.[140] As part of their investigation and study, PA Consulting interviewed both outside and in-house Ethicon experts. One such expert was Dr. Bernd Klosterhalfen, a KOL for Ethicon and consultant for 20 years. In his interview on January 18, 2011, Dr. Klosterhalfen informed PA Consulting and an Ethicon representative of many variables inherent in Ethicon's meshes that lead to patient complications and failures of the devices.[141] Regarding the shrinkage of Ethicon's meshes, Dr. Klosterhalfen restated what was known or should have been known for greater than a decade:

> At the high level, there are two classes of "shrinkage" observed with mesh implant (Note: the term 'shrinkage' is a misnomer. Tissue reaction over time encapsulates the mesh with connective tissue and effectively `crushes' the mesh into a ball (like crushing a sheet of paper); the mesh does not truly shrink):

---

[131] ETH.MESH.05446127 Email from Holste to Engel et al. re: Mesh and tissue contraction in animals
[132] ETH.MESH.05446127 Email from Holste to Engel et al. re: Mesh and tissue contraction in animals
[133] ETH.MESH.01218361-01218367: Dr. Kerstin Spychaj, State of the knowledge in "mesh shrinkage" – What do we know? 04/05/2007
[134] ETH.MESH.02992139 Lightning Clinical Strategy dtd 11/22/06
[135] Robinson deposition 03/13/12, 260:5-22
[136] Ciarrocca deposition 3/29/12, 340:9 to 340:12
[137] Kirkemo deposition 04/18/12, 105:14 to 108:16
[138] ETH.MESH.03924887 Meshes in Pelvic Floor Repair
[139] ETH.MESH.00870466 06/2/2006 Expert Meeting
[140] ETH.MESH.07192929 6/22/2011 PA Consulting "Investigating Mesh Erosion in Pelvic Floor Repair"
[141] ETH.MESH.07192412 PA Consulting meeting notes with Dr. Klosterhalfen

> - The first is in the immediate short term following implant; the implant is observed to lift and may 'roll up' from its position. This occurs as a result of poor positioning, placement and/or suturing of the implant by the clinician
>
> - The second class of shrinkage is the formation of scar tissue; observed in the longer term (months) following implantation. This scar tissue can reduce and compact, causing the mesh to crumple up.

That last quote is important because it documents what was known widely in mesh science and manufacturing industry since the 1990's; older, heavy weight, small pore meshes like the Prolene in Ethicon's TVT slings, increase the risk of mesh shrinkage or contraction – up to 50% of the area of the mesh. By this time in 2011, Dr. Klosterhalfen had received approximately 1,000 mesh explant samples over 10 years, and he and I had published a widely-circulated and discussed publication regarding our analysis of these 1,000 explants. He and I had also published a significant amount of peer-reviewed literature regarding explants, animal models and newer designs for more "ideal" meshes and had explained this phenomenon to Ethicon for many years as their consultants. Thus, in this interview, Dr. Klosterhalfen was simply restating what we had both studied in conjunction with Ethicon while researching safer mesh design with them since the early 1990's – all of their polypropylene meshes shrink from 30-50%, and the heavier the weight and smaller the distance between the fibers, the more this shrinkage phenomenon will occur.

It is my opinion, to a reasonable degree of medical and scientific certainty, based upon my background training and experience as a general and abdominal surgeon who used Prolene mesh for hernia repair in dozens of patients and treated Prolene-mesh-related complications in dozens of patients, and based on over 20 years of studying Prolene meshes, 10 years of which were as a consultant to Ethicon in developing safer mesh design and designing and carrying out their preclinical studies of Prolene and other surgical meshes, authoring or co-authoring numerous peer-reviewed publications regarding Prolene mesh, reviewing hundreds of internal Ethicon documents and hundreds of pages of deposition testimony that the mesh used in all of Ethicon's TVT sling products unnecessarily increases the risk of mesh shrinkage or contraction that in turn leads to an increased risk of intense and chronic FBR, severe and chronic inflammatory response, excessive scar formation, fibrotic bridging, increased risk of mesh encapsulation, scar plate formation, mesh shrinkage, nerve entrapment, chronic pelvic pain, erosions, chronic sexual dysfunction and dyspareunia, recurrence, inability to remove the device and need for painful and, at times, dangerous revision surgery and multiple, life-long, debilitating injuries in some women.

F. Fraying/Particle Loss/Curling/Roping/MCM/LCM

As discussed above, it is known that the TVT tape frays under minimal tension. In fact, one of Ethicon's Medical Directors noted in a memo and testified that fraying is inherent in the design of the mesh. [142] In that memo to file, he stated "Fraying is inherent in the design and construction of the product. The mesh elongates in places; the mesh narrows in places; and small particles of Prolene might break off." He also stated that the "stretching of the mesh increases the probability of fraying." [143] In 2000, surgeons in the field advised Brigitte Hellhammer, an

[142] ETH.MESH.00541379 Memo to File dtd 11/18/03 from Martin Weisberg Re: Mesh Fraying for TVT Devices
[143] Id.

Ethicon employee, that Ethicon's surgical mesh "released particles that migrate through the vaginal wall causing pain during intercourse".[144]

Then, in 2001, Dr. Alex Wang, who was described as "one of the most experienced TVT users in the world", informed Ethicon that he was having problems with frayed mesh and the uneven width of the sling. [145]

In November of 2003, Marty Weisberg, who at the time was the Senior Medical Director of Gynecare, made a note to the TVT file indicating that there had been 58 complaints of mesh fraying since 2000.[146] Also in 2003, Pariente published a study in which he evaluated the amount of material shed by different suburethral slings under certain test conditions.[147] Dr. Pariente's conclusion was that "the very high particle shedding for both SPARC (AMS) and TVT (Ethicon) may be of significant long term clinical concern in some quarters." TVT had the highest percentage loss of initial weight at 8.5%. Other authors have commented on the fraying phenomenon of Ethicon's TVT slings as well.[148]

The Pariente article then prompted the French regulatory agency, AFNOR to seek additional information from Ethicon regarding the high amount of particle loss. Ethicon Senior Scientist, Gene Kammerer believed that the method that AFNOR was requesting that they use in order to determine particle loss was unrealistic and too rigorous.[149] Kammerer, who is not a medical doctor, also stated that particle loss "is most likely an aesthetic issue".[150] However, information regarding the impact of particle loss on foreign body reaction and its clinical outcomes is concerning and required further study by Ethicon. These particles cause a greater risk for bacterial adherence[151] and increase the area of inflammatory response surrounding the implant in the tissues. There was insufficient medical and scientific data for this Ethicon scientist to simply state that there was no impact on clinical outcomes of this loss of particles without any scientific or clinical testing to support such a statement. Ethicon's Medical Director, Dr. Martin Weisberg, confirmed in his deposition that he was not sure whether or not particle loss and fraying would lead to clinical implications and did not know if Ethicon ever tested particulates for clinical implications.[152] One such implication was a report to Ethicon by a TVT surgeon whose patient had erosion into her vaginal wall following implantation with a TVT sling.[153] The patient's husband reported that during sexual intercourse the "tape appeared frayed and tiny fibers were protruding through the vaginal wall".

In 2004, Ethicon received clinical reports from other surgeons who were using their TVT products of this "crumbling" mesh problem. One of their surgical consultants informed the company that "it is embarrassing to see how the tape is crumbling" and it "gets worse if there is a

---

[144] ETH.MESH.03924557 Meshes in Pelvic Floor Repair
[145] ETH.MESH.03905472
[146] ETH.MESH.01126906
[147] ETH.MESH.01221055 Pariente J-L; An independent biomechanical evaluation of commercially available suburethral slings. Issues in Women's Health
[148] Moalli P, Papas N, Menefee S, Albo M, Meyn L, Abramowitch D; Tensile properties of five commonly used mid-urethral slings relative to TVT. Int Urogynecol J (2008) 19:655-663
[149] ETH.MESH.00583446 5/4/06 email from Gene Kammerer re French Regulatory and Particle Loss
[150] ETH.MESH.0058448 email re Urethral Sling particle loss standards and AFNOR
[151] Jongebloed WL. Doc Ophth 1986; 64:143, Sternschuss G. J Urol 2012; May 12 epub, Clave A. Int Urogyn J 2010; 21:261
[152] Weisberg deposition 5/31/13, 469:23 to 470:16
[153] ETH.MESH.02622276 TVT Complaint

stretch on the tape". This Ethicon consultant, Dr. Eberhard stated "the quality of the tape is terrible" and "I can't understand that no one will solve the problem for such a long time". [154, 155]

Austrian Ethicon surgical consultants had also reported problems with fraying and particle loss. An email in 2004 detailed the problem that a preceptor for TVT training in Austria was having when he "noticed that small blue particles kept falling off the mesh, as if the mesh was as he put it 'brittle'".[156] The email states that "[s]ince our mesh is now blue, would it be possible that this was always the case but now it is simply visible as opposed to before the introduction of TVT Blue?" In a later email in that string, Dan Smith stated "I believe the board has to set a directive that can be filtered down to the reps, saying it's OK and it's not an issue, same as TVT clear except you can see it. By the way you can also see it in the package as the pieces fall out of the sheath splits!" He then sates what appears to be a pattern in Ethicon's reaction to reports from surgeons regarding problems with the TVT mesh: "This is not going away anytime soon and competition will have a field day, major damage control offensive needs to start to educate the reps and surgeons UPFRONT that they will see BLUE shit and it is OK."

A Canadian KOL, in fact, the highest volume user of TVT in that country, Dr. Kenny Maslow complained to Ethicon about the fraying of their mesh down to a thin fiber even with "very little tension applied to the sling".[157]

[154] ETH.MESH.02180833 Translation of Eberhard Letter
[155] ETH.MESH.02180828 Eberhard complaint
[156] ETH.MESH.06881079 Email from Dan Smith re Important: 2 TVT Complaints concerning allegedly brittle mesh
[157] ETH.MESH.12910023

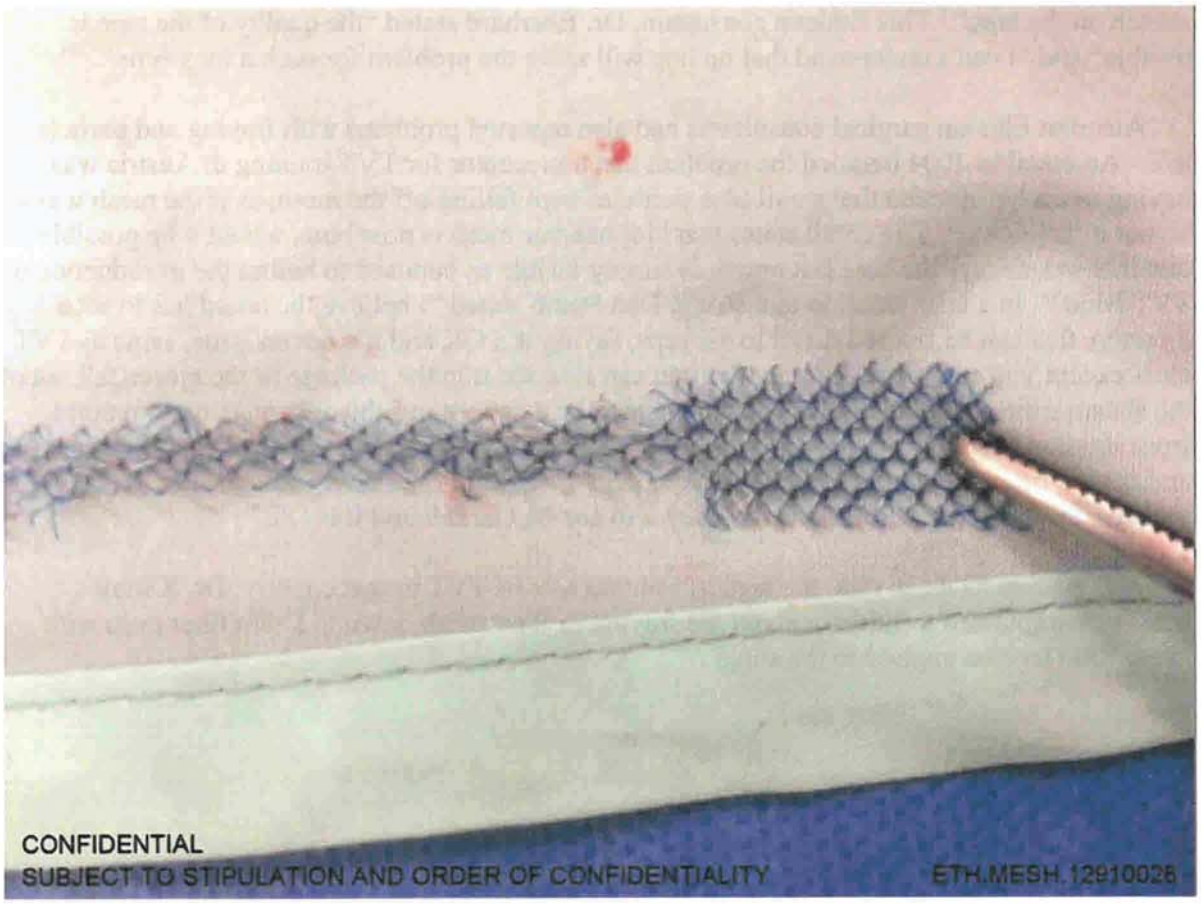


Figure 17[158]

Correspondence indicates that Ethicon was attempting to move Dr. Maslow to the TVT-Abbrevo sling, which is only offered in laser cut mesh, and Dr. Maslow informed Ethicon that he was interested in laser cut edges for the TVT-O product has he was still having many of them "frey" down to a thin fiber sling with very little tension applied. This is consistent with feedback from surgeons in 2006, who told Ethicon that the TVT Laser cut mesh is smoother and has less rough edges that the mechanically cut TVT mesh.[159] One surgeon told Ethicon that the mechanically cut strips had fraying "hairs" on the edges that scratched with abrasive texture scraping like Scotch-brite pads. Multiple surgeons in 2006 told Ethicon that a rope-string effect could occur if force was applied to the mechanically cut mesh, just as Dr. Maslow experienced and documented with photographic evidence in 2013. Ethicon also received feedback from customers and regulators that the edges of the TVT mesh appear to be sharp and likely to cut tissue.[160]

[158] ETH.MESH.12910023
[159] ETH.MESH.06696589
[160] ETH.MESH.00330760

While Ethicon employees such as Gene Kammerer believed this fraying and particle loss to be "an aesthetic issue", actual TVT surgeons, including Ethicon consultants, obviously believed differently. However, Ethicon chose to continue to sell their TVT mesh as it was with no design changes to address the problem. Instead, members of the sales and marketing team at Ethicon were instructed to tell doctors that "Prolene is proven to be inert"; that "the particles will not cause any problem"; and that the sales representatives should be "proactive" because "the competition will try to target this!"[161] Ethicon's position during this time was that the particles were not reactive and created no risk to patient safety.[162]

MCM/LCM

In 2005, Ethicon attempted to address the problem of the fraying of TVT mechanical cut mesh ("MCM") by instituting a new method of cutting its TVT mesh called laser cutting ("LCM").[163] At first, Ethicon's design engineers evidently felt that testing for critical design considerations like particle loss, flexural rigidity and elongation at various forces was not "critical to quality" and stated this in internal documents as "!!!!!GREAT NEWS FOR TVT LASER CUT MESH!!!!!" and "less work for all of us."[164] Ethicon had evidently determined that although there was greater particle loss with MCM, their test results showed that the difference was not significant enough to be concerned.[165]

The 2006 Clinical Expert Report for TVT LCM indicated that LCM had decreased particle loss from MCM and that this "decrease would lead to less non-functioning material left in the tissues". [166] There simply is no patient benefit to excess, "non-functioning" polypropylene in a woman's pelvic tissues. More fibers migrating in the tissues create an additional foreign body reaction and inflammatory response at the site of each piece of TVT mesh fiber in the body causing an increased risk of harm to patients, including chronic pain.

Ethicon considered the hazards and resulting harms in a woman's pelvic tissue due to roping, rough/frayed edges, pore deformation and other possible design failures of the TVT device in its dFMEA for LCM in 2006. [167] Ethicon admits that one of the primary functions of performing a harms/hazards design risk assessment is patient safety.[168] The Medical Affairs Director for the dFMEA, David Robinson, testified that these were in fact the considerations by the Ethicon team charges with completing the dFMEA.[169]

In elongation studies conducted by Ethicon in 2004 comparing its MCM and LCM TVT meshes to competitor meshes, Ethicon used an Instron machine (using uniaxial forces) to stretch the meshes to 20% elongation.[170] Ethicon scientists concluded that "[c]utting the TVT mesh with

---

[161] ETH.MESH.00865322 email from Charlotte Owens re Reminder on Blue Mesh!
[162] ETH.MESH.03535750 Letter to Herve Fournier re TVT Device, Blue Mesh; ETH.MESH.00541379 Memo re Mesh Fraying to TVT Devices; ETH.MESH.00858252: Memo re Mechanical Cut vs. Laser Cut Mesh Rationale
[163] ETH.MESH.00301741 email from Daniel Lamont re !!!!Great News for TVT Laser Cut Mesh!!!!; ETH.MESH.00394544: Global Regulatory Strategy – GYNECARE TVT – Laser Cutting Project memo; Weisberg deposition 05/31/2013, 487:13 to 488:7
[164] ETH.MESH.00301741; Weisberg deposition 05/31/2013, 490:15 to 491:17
[165] ETH.MESH.01219984 Completion Report for the Design Verification of TVT Laser Cut Mesh; ETH.MESH.00585842 Email from Gene Kammerer re TVT LCM – Particle loss
[166] ETH.MESH.00167109 Martin Weisberg Clinical Expert Report: Laser Cut Mesh for TVT
[167] ETH.MESH.012180109 DFMEA
[168] Smith deposition 06/04/2013 654:1 to 655:20
[169] Robinson deposition 09/11/2013 1070:23 to 1072:25
[170] ETH.MESH.01809080 Comparison of Laser-Cut and Machine-Cut TVT Mesh to Meshes from Competitive Devices (BE-2004-1641)

a laser rather than a machine does not impact the established relationship between TVT and its competitors with regard to tensile behavior at low (20%) elongation."

In 2006, Gene Kammerer performed comparisons of LCM to MCM.[171] He placed samples of LCM and MCM TVT mesh under strain to 50% elongation and found that the MCM samples showed "degradation of the structure of the mesh in certain areas where, because of particle loss, the knit has opened and a portion of the construction has been lost. The area may also be stretched and narrowed resulting in roping due to this occurrence." The LCM sample also showed stretching and narrowing, "but is generally less than the MCM". [Fig. 18]

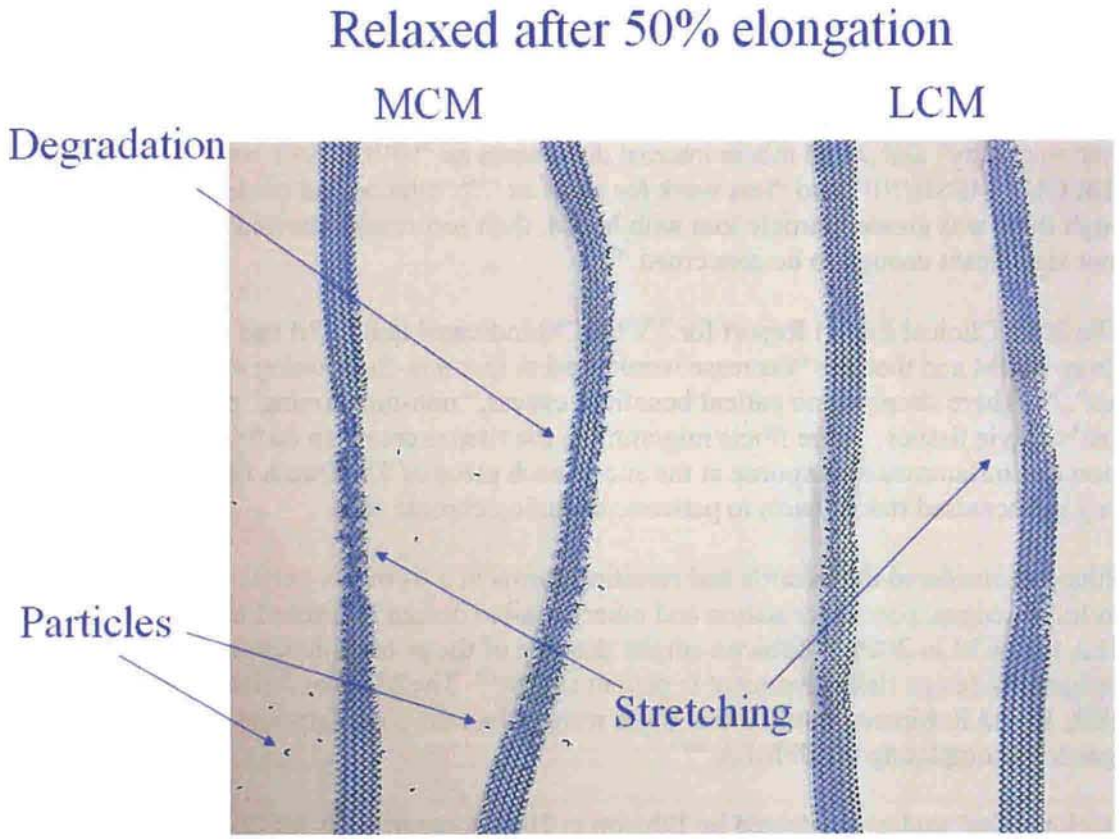


Figure 18

Mr. Kammerer stated in internal documents that according to his experience "viewing many surgical procedures and performing numerous procedures on cadavers myself, that the mesh stretches approximately 50% at the maximum".[172]

[171] ETH.MESH.08334244 email from Gene Kammerer re Photographs of LCM vs. MCM
[172] ETH.MESH.00584811

Ethicon Medical Affairs director, David Robinson, admitted at his deposition that the stiffer LCM TVT was intended to address the problems noted by Mr. Kammerer in his internal studies. He testified that "customers were expressing they wanted a change with the particle loss, roping, change in tension during sheath removal" and admitted that one of the goals of LCM was to prevent roping and that roping was due to the elasticity problem with MCM TVT.[173] Ethicon's internal failure modes and analysis demonstrated that the potential for roping, curling and frayed edges could cause erosions, pain and recurrence.[174]

Despite these internal test results and recognition of the problems associated with the Prolene MCM mesh utilized in the TVT devices, upon developing the LCM Prolene mesh, Ethicon continued to sell BOTH products simultaneously. In an internal Ethicon email dated May 6, 2005, Ethicon Product Director, Allison London Brown, stated "[t]he basic story here is that the current mesh (MCM) is perceived by some physicians as inferior and we do get a high number of complaints on linting [fraying][175] and roping (mesh particles falling off and the material stretching to the point of being a string). The new material will dramatically reduce the incident of linting [fraying] and should all but eliminate the roping as it stays nice and flat". [176] Ms. Brown asked for her Ethicon colleagues to help her "craft" a story for its TVT customers (surgeons) to "reduce confusion and complexity" and to "tell a nice story without overly admitting that the current procedure may some have perceived aesthetic problems (not clinically relevant problems)."

Other Ethicon employees had similar marketing strategies/concerns in mind. Ethicon U.S. Group Product Director, Kevin Mahar, in an email dated May 24, 2005 had this to say regarding positioning both TVT products in the market at the same time: "Positioning? While we would work with our agency to get this right, my thoughts are we KEEP selling regular TVT (the Colonel's "Original Recipe") to those customers that want/love it…and KEEP going forward with 8 years of data, etc. with the original recipe…we simply ADD these 2 LCM codes and if we have customers demanding LCM, we say, here you go! We do not mislead them that this is the same product, we simply say '…from the makers of TVT…the company 'built' on a tradition of trust, blah, blah, blah')".[177] Earlier in that email string, Ms. Brown stated that the marketing strategists inside Ethicon had "some discussions on the Laser-cut mesh and the impact to base. Most definitely we need to understand how we globally utilize the material and take advantage of the new product, without detriment to the Base business."

In other internal Ethicon emails, Dan Smith from R&D explains that the TVT and TVT-O meshes cause more urinary retention than its TVT-Secur product because the TVT and TVT-O products "curl and rope which reduces the surface area of the mesh under the urethra and therefore, increases the pressure in a localized point". [178] At the deposition of yet another Ethicon employee, Dan Lamont, he confirmed Mr. Smith's statements saying "[t]here is a potential for roping to occur on the TVT mechanically cut mesh" but "Ethicon chose to continue to sell mechanically cut mesh".[179] The top complaint of TVT surgeons from 2003-2006 was

---

[173] Robinson deposition 07/25/2013 492:10 to 493:19
[174] ETH.MESH.01218019
[175] Robinson deposition 07/25/2013 502:21-503:1
[176] ETH.MESH.00526473 Email from Allison London Brown re Laser-Cut mesh
[177] ETH.MESH.00687819 Email from Kevin Mahar re Laser cut mesh
[178] ETH.MESH.01822361 Email from Dan Smith re TVT Secur
[179] Lamont deposition 09/11/2013 25:8 to 25:20; 35:19-36:4

"Mesh Fraying/Roping".[180] (I have viewed an Ethicon TVT implantation DVD which confirms Mr. Lamont's observations that even during the implant procedure, one can see the deformed pores and narrowing of the sling above the scissors and below the urethra while tensioning the sling intra-operatively). [181]

It is my opinion, to a reasonable degree of medical and scientific certainty that the TVT mesh is a knitted textile design without a sealed border and therefore, it has frayed edges that tend to shed particles of polypropylene before, during and after the surgery. As tension is placed on the mesh, it curls, ropes and sheds these particles, all of which makes the TVT Mechanical-cut mesh (MCM) unreasonably and unnecessarily unsafe for its intended purpose of being permanently implanted in a woman's pelvic tissues as an anti-incontinence device. The curled, frayed, sharp edges and the dislodged, migrating particles of the TVT MCM products increase the risk of increased inflammatory response, chronic foreign body reaction, erosions, chronic pelvic pain, failure of the implant, dyspareunia, organ damage, urinary dysfunction and the need for surgical intervention.

VII. SAFER ALTERNATIVE DESIGN

There are alternative design characteristics that would be safer in a woman's pelvic tissues as a treatment for incontinence than some of the design characteristics of the Prolene mesh in TVT. One such safer alternative design would be a mesh product with less material and larger distance between the mesh fibers (Ethicon's Ultrapro mesh has 3-5mm between the fibers and has a weight of 25 g/m2).

Another safer design would be a polymer that elicits a more favorable inflammatory response. PVDF, as a synthetic, non-absorbable suture or mesh material has improved textile and biological properties over polypropylene. It is thermally stable and more abrasion resistant than other flouroplastics and induces a minimal cellular response, shows exceptional chemical stability and has excellent resistance to aging. PVDF sutures are routinely used in cardiovascular and orthopaedic surgery.[182]

In 1998, with the support of Aachen University, I started a research project to develop a monofilament mesh made of pure PVDF, as it was suspected to be the best polymer available at that time. Ethicon supported our study by providing us with one of their PVDF meshes for testing in an animal experiment. Our study showed that the PVDF material had a better performance in the tissue than Prolene. The results were presented to Ethicon in 2001 and were published in 2002.[183] However, upon presenting the results to Ethicon, they rejected any further collaboration with our research group to develop meshes of PVDF with the comment that there was no interest by Ethicon to replace their polypropylene meshes with PVDF.

Despite telling me and our group that Ethicon had no interest in working with us to develop a PVDF surgical mesh, in 2000, Ethicon had received 510(k) clearance in the United States for a

---

[180] ETH.MESH.00302390 TVT-Base & TVT-O Review for Laser Cut Mesh (LCM) Risk Analysis
[181] ETH.MESH.PM.000004 TVT Retropubic Implantation Video
[182] Laroche G, Marois Y, Guidoin R. Polyvinylidene fluoride (PVDF) as a biomaterial: from polymeric raw material to monofilament vascular suture. J. Biomed. Mater. Res. 1995; 29:1525-1536
[183] PVDF as a new polymer for the construction of surgical meshes. Klinge U, Klosterhalfen B, Ottinger AP, Junge K, Schumpelick V. Biomaterials. 2002 Aug;23(16):3487-93)

PVDF suture. The product name was "Pronova".[184] In 2002, Ethicon obtained a German patent No. DE 10043396C1 20.06.2002 for a PVDF surgical implant, including requirement of pore sizes of > 1.5 mm.[185] The advantage of a PVDF device was explained by studies listed in the patent.[186] Those studies, as well as some of which that I have published, have shown that this material has improved textile and biological properties.[187, 188]

In an email from a top Ethicon German scientist in 2007 regarding internal reaction to recently-published literature concerning degradation of polypropylene meshes in human tissue explants, Dr. Dieter Engel stated, "What is the future? We will change the material of our mesh and move to Pronova as the future material platform for mesh…Pronova has a reduced foreign body reaction compared to Prolene, as shown in several animal studies, and will improve the perceived biocompatibility of our mesh. Besides, Pronova is much less susceptible to mechanical damage…it is much easier to process in the knitting machines, less quality issues."[189]

Ethicon reveal that they funded internal studies to develop Pronova (PVDF) sutures as a prolapse mesh. They investigated this PVDF pelvic floor repair design concept through a new project dubbed by Ethicon as "Project Thunder". In the August 14, 2007 Project Thunder meeting minutes, Ethicon scientists reported the progress of the project and listed the pros and cons of Pronova to polypropylene as follows: Pro: Softness, Elasticity, better biocompatibility, less "aging"/long time breakage, easier to manufacture and sterilize. Con: "May be more expansive [sic]".[190] Other Ethicon documents also focused on the fact that Ethicon determined that PVDF would cost more than polypropylene.[191, 192] In a May 9, 2008 Project Thunder presentation, one slide is particularly telling. It shows the PVDF products all out-performing Ethicon's polypropylene meshes in every design attribute except one…cost.[193] Project Thunder was "killed" by Ethicon despite the fact that at multiple meetings, it was described as the "holy grail" of pelvic floor meshes, the first "patient-centric" mesh, the first Ethicon mesh actually "designed for the pelvic floor" and explained that it would address the concern by Ethicon that its surgical meshes at the time that were all "overengineered".[194]

It has been found in literature that polypropylene degrades and PVDF does not. This can be found in numerous articles, by numerous authors. Numerous other articles have demonstrated the superior benefits of PVDF in tissue.[195, 196, 197, 198, 199]

---

[184] ETH.MESH.01819833 "Pelvic Floor Repair Platform" Slide 35
[185] German Patent No. DE10043396C1 20.06.2002; Certified Translation of Patent
[186] German Patent No. DE10043396C1 20.06.2002; Certified Translation of Patent
[187] Klinge U, Klosterhalfen B, Ottinger A, Junge K, Schumpelick V. PVDF as a new polymer for the construction of surgical meshes. Biomaterials 2002; 23:3487-3493
[188] Klink C., Junge, J., Binnebosel., Alizai, H., Otto, J., Neumann, U., Klinge, U. Comparison of Long-Term biocompatibility of PVDF and PP meshes. Journal of Invetigative Surgery (2011); 24:292-299
[189] ETH.MESH.05447475 Email from Dieter Engel to John Gillespie et al. re How inert is polypropylene?
[190] ETH.MESH.00869908 Thunder Meeting Minutes dated 8/14/07
[191] ETH.MESH.02227224 PowerPoint Presentation dated 05/09/08 titled MGPP Thunder Decision Meeting
[192] ETH.MESH.00869908 Thunder Meeting Minutes dated 8/14/07
[193] ETH.MESH.02227224 PowerPoint Presentation dated 05/09/08 titled MGPP Thunder Decision Meeting
[194] ETH.MESH.00562421 untitled PowerPoint updated from November 2010-October 2011
[195] Klink C., Junge, J., Binnebosel., Alizai, H., Otto, J., Neumann, U., Klinge, U. Comparison of Long-Term biocompatibility of PVDF and PP meshes. Journal of Invetigative Surgery (2011); 24:292-299
[196] Silva, R., Silva, P., Carvalho, M. Degradation Studies of Some Polymeric Biomaterials: Polypropylene (PP) and Polyvinylidene Difouride (PVDF). Material Science Forum (2007); 593-543
[197] Conze, J., et al., New polymer for intra-abdominal meshes--PVDF copolymer. J Biomed Mater Res B Appl Biomater, 2008. 87(2): p. 321-8.
[198] Klinge U, Klosterhalfen B, Ottinger A, Junge K, Schumpelick V. PVDF as a new polymer for the construction of surgical meshes. Biomaterials 2002; 23:3487-3493
[199] Laroche G, Marois Y, Guidoin R. Polyvinylidene fluoride (PVDF) as a biomaterial: from polymeric raw material to monofilament vascular suture. J. Biomed. Mater. Res. 1995; 29:1525-1536

The characteristics of implanted polyvinylidene fluoride and polypropylene sutures used in vascular surgery were analyzed in 1998 by Celine Mary et al. They found that after periods of 1 and 2 years there was little to no sign of surface cracking of polyvinylidene fluoride whereas explanted polypropylene sutures showed visual evidence of surface stress cracking. The authors concluded that the PVDF likely has superior biostability to polypropylene over the long term. [200]

Klink et al. compared the performance of PVDF and polypropylene meshes. The SEM data clearly suggests degradation on the part of polypropylene mesh with virtually none found in the PVDF mesh after implantation in rats. They concluded that PVDF meshes show low inflammation and mature scar formation after six months and that PVDF would be a possible alternative to polypropylene mesh implants. [201]

In fact, even in Ethicon's own 7-year dog study, conducted in the late 1990's, it was found that after seven years, Ethicon's Prolene sutures showed progressive degradation, while PVDF sutures showed none. [202]

Our published studies regarding the structural stability of meshes under various stresses in 2013 and 2014 have shown superior characteristics of mesh made of PVDF versus Ethicon's surgical meshes.[203] Overall, the alternative textile structure made of PVDF (product name "Dynamesh") showed remarkable effective porosity and high effective porosity persisting even under strain whether the measurements were taken in the center portion of the prosthetic or in the arm. It also showed roughly equivalent performance under strain whether being tensed in the warp or cross direction. In sum, Dynamesh showed excellent structural stability under tension and excellent effective porosity to resist fibrotic bridging. Another significant observation of the Dynamesh product is that unlike Prolift, Dynamesh has a smooth seam around the entirety of the mesh with no fraying at the edges nor curling in the arms under strain as was seen with both of the Ethicon products.

At his deposition, Dr. Holste was asked about Ethicon activities involving comparing their products to Dynamesh. According to Ethicon documents, they were examining Dynamesh's manufactuer, FEG's website and trying to determine if they could disprove any of FEG's claims regarding their meshes, including Dynamesh. Ethicon field representatives in Brazil were so concerned about the competition by Dynamesh sling products in that country that in 2009, they were sending emails regarding how to disparage FEG's product to keep them from using Dynamesh. [204]

In addition to the Dynamesh products, there are a number of other meshes made with sealed borders that are on the market and sold in the U.S. The technology of weaving a seam or a sealed border on textiles has been available for many, many decades and therefore, such technology existed before woven polypropylene surgical meshes for the pelvic tissue (i.e., slings

---

[200] Celine Mary, Yves Marois, Martin W. King, Gaetan Laroche, Yvan Douville, Louisette Martin, Robert Guidoin, Comparison of the In Vivo Behaviour of Polyvinylidene Fluoride and Polypropylene Sutures Used in Vascular Surgery, *ASAIO Journal*, 44 (1998) 199-206

[201] C. D. Klink, K. Junge, M. Binnebosel, H. P. Alizai, J. Otto, U. P. Neumann, U. Klinge, Comparison of Long-Term Biocompability of PVDF and PP Meshes, *Journal of Investigative Surgery*, 24 (2011) 292-299.

[202] ETH.MESH.09557798 7 Year Dog Study

[203] Otto, J., Kaldenhoff, E., Kirschner-Hermanns, R., Muhl, T., Klinge, U. Elongation of textile pelvic floor implants under load is related to complete loss of effective porosity, thereby favoring incorporation in scar plates. Wiley Online

[204] ETH.MESH.04066979 Email re Dynamesh in Brazil

and POP mesh) were sold on the market beginning in 1997. As such, and to a reasonable degree of medical and scientific certainty, the open, unsealed borders of Gynemesh PS, unnecessarily increase the risk of patient complications and injuries. There were and are safer alternative mesh designs to Gynemesh PS that would have eliminated and/or drastically reduced this risk.[205]

Based on these characteristics, my studies comparing PVDF to polypropylene, Ethicon's internal documents and other scientific literature, as well as my background, training and experience over 30 years, it is my opinion, to a reasonable degree of medical and scientific certainty, that PVDF, in the appropriate design, is a safer alternative mesh material for treatment of stress urinary incontinence than Ethicon's TVT Prolene mesh.

VIII. PREVIOUS TESTIMONY

On November 4, 2015, my trial deposition testimony was given in *Mullins et al v. Ethicon, Inc., et al.*. All of my opinions and testimony contained within that transcript are incorporated herein by reference and attached as Exhibit "C". Additionally, as noted in Section X below, I have given testimony and provided expert reports in numerous Ethicon transvaginal mesh cases over the past few years. All of my testimony and opinions therein are hereby incorporated by reference.

I reserve the right to modify these opinions as necessary based upon any new or additional information or data that I may obtain or with which I am presented including, without limitation, any materials that I produce in response to Ethicon's requests.

IX. EXHIBITS

My current curriculum vitae is attached as Exhibit "A"

All exhibits that will be used to support my finding and opinions are included above and listed below in Exhibit "B"

November 4, 2015 De Bene Esse Transcript attached as Exhibit "C"

Gross Expert Report attached as Exhibit "D"

Gross deposition attached as Exhibit "E"

Gross Trial Testimony as Exhibit "F"

Lewis Expert Report attached as Exhibit "G"

Lewis deposition attached as Exhibit "H"

Lewis Supplemental Expert Report "I"

Lewis Trial testimony attached as Exhibit "J"

Bellew Expert Report attached as Exhibit "K"

---

[205] Trial testimony taken 11/10/14 and 10/04/15

Bellew Trial Testimony attached as Exhibit "L"

Corbet/Watkins Expert Report attached as Exhibit "M"

Huskey/Edwards Expert Report attached as Exhibit "N"

Mullins Expert Report attached as Exhibit "O"

Mullins deposition attached as Exhibit "P"

X. RECENT TESTIMONY/EXPERT HISTORY

Linda Gross, et al. vs. Gynecare, et al.; Superior Court of New Jersey Law Division – Middlesex County Case No. MID-L-9131-08

Carolyn Lewis v. Ethicon, Inc., et al.; Southern District of West Virginia Charleston Division Case No. 2:12-cv-04301

Dianne M. Bellew v. Ethicon, Inc., et al.; Southern District of West Virginia Charleston Division Case No. 2:13-CV-22473

Kathryn Corbet et al. vs. Ethicon, Inc. et al.; Superior Court of New Jersey Law Division – Atlantic County Case No. ATL-L-2911-13 – Report Only

Dale Watkins et al. vs. Ethicon, Inc. et al.; Superior Court of New Jersey Law Division – Bergen County Case No. BER-L-13787-14 MCL – Report Only

Jo Huskey (2:12-cv-05201). Report Only

Tonya Edwards (2:12-cv-09972). Report Only

Mullins et al v. Ethicon, Inc., et al.; Southern District of West Virginia Charleston Division Case No. 2:12-cv-02952

XI. COMPENSATION

I am compensated for investigation, study and consultation in the case at the rate of $500.00 per hour.

This 16th day of November, 2015

Prof. Dr. med. Uwe Klinge